

From Center for Family and Community Medicine, CeFAM
Department of Neurobiology, Care Sciences and Society
Karolinska Institutet, Stockholm, Sweden

DIABETES AMONG TURKISH IMMIGRANTS IN SWEDEN

A study of prevalence and risk factors

Kristín Hjörleifsdóttir Steiner



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*In memory of my parents, my mother Björk
Gudmundsdóttir and father Hjörleifur Björnsson,
for bringing spirituality and music into my life.*

*“Nothing will sustain you more potently
than the power to recognize in your humdrum
routine, as perhaps it may be thought, the true
poetry of life—the poetry of the commonplace, of
the ordinary man, of the plain, toil-worn woman,
with their loves and their joys, their sorrows and
their griefs.”*

- Sir William Osler

ABSTRACT

Background Risk factors associated with the difference in susceptibility to diabetes in different ethnic groups are poorly understood. This thesis investigates differences in prevalence of, as well as risk factors for, diabetes, impaired glucose tolerance (IGT) and impaired fasting glucose, and whether there is an effect of migration, in Turkish immigrants in Sweden.

Methods Two data sets were used for this thesis, a survey from the Swedish National Board of Health and Welfare (the Immigrant Survey) combined with the Swedish Survey of Living Conditions and a cross-sectional total-population survey on Turkish immigrants in Flemingsberg, Sweden. From the first survey, data were compared between Turkish immigrants in Sweden (n=526) and Swedish controls (n=2,854), all in ages 27-60 years. The second survey, which included a questionnaire, a medical examination, an oral glucose tolerance test (OGTT) and other laboratory analyses, comprised 238 Turkish men and women aged ≥ 20 years, living in Sweden. Data on diabetes and IGT were compared with 1549 participants of the same age, living in the Konya area in Turkey. Risk factors studied in the Turkish group in Flemingsberg were hypertension, obesity, central obesity, high fasting triglycerides, low HDL cholesterol, the metabolic syndrome, smoking and alcohol consumption, physical inactivity, stress, poor self-rated health and socio-economic factors.

Results The self-reported diabetes prevalence was higher among Turkish women in Sweden, odds ratio (OR) 3.22, 95% confidence interval (CI) 1.36-7.64, compared to Swedish women. After adjustment for low educational level, unemployment and increased BMI, there was no difference between groups. Self-reported stress (anxiety, sleeping problems and pain) was also more common among Turkish men and women (compared to Swedish controls) even after adjusting for socio-economic factors.

The prevalence of diabetes and IGT, was significantly higher among Turkish immigrants in Flemingsberg (11.8% and 15.6%, respectively), compared to controls in Turkey (7.1% and 7.6%, respectively). Turkish women in Sweden had a significantly higher prevalence of diabetes than Turkish women in Turkey (12.8% vs. 7.6%) and IGT was significantly higher among Turkish men in Sweden compared to men in Turkey (17.8% vs 4.9%). Mean onset of diabetes in the Turkish group in Flemingsberg was at 47 years. The fully adjusted odds of Turkish men in Flemingsberg having DGT (Disturbed Glucose Tolerance = diabetes or IGT) were 4-5 times higher if they had hypertension or were smokers or former smokers. Among women risk factors were central obesity and high fasting triglycerides (4.5 times higher odds for DGT). Men who reported smoking and alcohol consumption, were 3 times more likely to be newly diagnosed with DGT (OR 3.58, CI 1.29-9.96). Odds for newly diagnosed DGT were also higher among employed Turkish women in Flemingsberg (OR 2.73, CI 1.05-7.05). There was no association between DGT or the Metabolic Syndrome, with stress factors.

Conclusions Turkish immigrants in Sweden are a risk group for diabetes. Culturally adjusted and gender specific intervention programs are urgently needed. Overweight, hypertension, alcohol consumption and smoking should be targeted risk factors. Identification of acculturation factors, such as changes in lifestyle, vitamin D-deficiency or change in microbiota is an important field of research to explain changing risks of diabetes among immigrants.

LIST OF PUBLICATIONS

This thesis is based on the following original articles, which will be referred to in the text by their Roman numerals.

- I Diabetes mellitus in Turkish immigrants in Sweden**
PE Wändell, K Hjörleifsdottir Steiner, SE Johansson. Diabetes Metab 2003, 29, 435-9

- II Self-Reported Anxiety, Sleeping Problems and Pain Among Turkish-Born Immigrants in Sweden**
Kristin Hjörleifsdottir Steiner, Sven-Erik Johansson, Jan Sundquist & Per E. Wändell. Ethnicity and Health, 2007, Vol. 12, No. 4, pp. 363-379

- III Diabetes and impaired glucose tolerance among Turkish immigrants in Sweden**
K. Hjörleifsdottir-Steiner, I. Satman , J. Sundquist , A. Kaya , P. Wändell
Diabetes Research and Clinical Practice, 2011, Vol 92, Issue 1, Pages 118–123

- IV Risk factors for disturbed glucose tolerance among Turkish immigrants in Sweden**
K. Hjörleifsdottir-Steiner, P. Wändell, J. Sundquist. Manuscript submitted

- V Stress Factors and their association with disturbed glucose tolerance among Turkish immigrants in Sweden**
K. Hjörleifsdottir-Steiner, P. Wändell, J. Sundquist. Manuscript submitted

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LIST OF ABBREVIATIONS

ADA	American Diabetes Association
ATPIII	Third Adult Treatment Panel
BMI	Body Mass Index
CHD	Coronary Heart Disease
CI	95% confidence interval
CVD	Cardio Vascular Disease
DGT	Disturbed Glucose Tolerance
FBG	Fasting Blood Glucose
FPG	Fasting Plasma Glucose
GDM	Gestational Diabetes Mellitus
HDL	High density lipoprotein
HT	Hypertension
IDF	International Diabetes Federation
IFG	Impaired Fasting Glucose
IGT	Impaired Glucose Tolerance
IHD	Ischaemic Heart Disease
OGTT	Oral Glucose Tolerance Test
OR	Odds Ratio
SRH	Self Rated Health
TG	Triglycerides
WHO	World Health Organization

PREFACE

How did this all start? I was just about to become a paediatrician when a colleague of mine (a paediatrician who became a general practitioner), asked if I could consider working as a general practitioner in Flemingsberg, a neighbourhood with many young immigrant families. It was difficult to hire doctors to this deprived area and I was asked to stay until the situation at the primary health care centre was more stable. After that I could return finishing my speciality training in paediatrics. What was supposed to be a summer, became years, I left the paediatric field and decided to specialize in general medicine and to continue working in Flemingsberg where I met fascinating patients from all over the world. After some time, several questions about my patients' health situations arose. As I got to know the patients, I gradually received knowledge about the diverse cultural aspects of symptoms presented to me, for example the taboos and cultural ways to express distress that led to somatising ill health that was obviously of mental origin. However, it struck me that many of my patients, especially the Turkish group, had overweight, obesity, diabetes and general pain. Pain in the neck, shoulder and back was one of the main reasons for sick leave and a great burden for the Turkish group especially the women who often described their work as heavy. How come so many were overweight? Why did I meet so many with diabetes and at quite young age? Could there be a connection between diabetes and pain? Was there some kind of stress or distress? What role did the migration play? Did poor acculturation contribute? Did the people in their home country experience the same poor health?

Equal health care does not mean the same health care to everyone, it means providing a personalized care in dialogue with the patient. How was I prepared for that? Was intervention for diabetes, based on research on Swedish groups suitable for my Turkish patients? Perhaps we were dealing with a kind of type 2 diabetes that is different to the type 2 diabetes seen in the Swedish population? Our practical knowledge from diet-groups at the primary health care centre was that the Turkish group had difficulties losing weight. We also noticed a growing prevalence of overweight children in this group. How was the diet? How about the physical activity? Was this a result of the rural-to-urban change of lifestyle with adopting an unhealthy lifestyle?

How could I investigate all of this? Was there a reasonable possibility to design a holistic and general project, combining medicine and public health with a bit of sociology, anthropology and epidemiology? Filled with questions, curiosity and a fascination for the Turkish immigrant group in Flemingsberg I decided to contact the research centre of family medicine. I met Professor Per Wändell and this thesis is the result of our meeting.

1 INTRODUCTION

There is no doubt that the world is facing an emerging diabetes epidemic. The complications from diabetes in several organ systems are of major concerns for health care planners worldwide. Patients with type 2 diabetes have a two to four times higher risk of coronary heart disease than the rest of the population, their prognosis is poorer, 75–80% will die of cardiovascular disease and the premature mortality is estimated to 12–14 years of life. Diabetes and its complications with cerebrovascular, peripheral vascular, and kidney disease, as well as neuropathy cause suffering among 200-300 million people and the direct health care costs range from 2.5% to 15% of annual health care budgets, depending on local diabetes prevalence and the sophistication of the treatments available. Many of the complications are potentially preventable or possible to delay given prompt diagnosis of diabetes, comprehensive and continuous care, effective patient and professional education [1-3].

It is well known that the prevalence, onset and progression of diabetes vary between different ethnic groups, depending on the predisposed vulnerability. In 2004, approximately 12 % of the population in Sweden were foreign-born. Migration to a socially and culturally different society is likely to be stressful and can cause dramatic life changes, where difficulty in acculturation or acculturative stress could affect mental and physical health, e.g., add to the risk of developing diabetes. On the other hand, the acculturation process might also result in the abandoning of health-promoting behaviour while adopting the less healthy habits of the adopting society. This could result in a rate of illness not only equal to the rates found in the receiving country and country of origin, but higher, as a result of the interaction between genetic predisposition and environmental factors. Many migration studies have pointed out this vulnerability among immigrants. In the perspective of public health, it is of outmost importance to analyse and clarify differences in health between populations and whether ethnicity, genetic disposition in combination with migration might play an important role. This knowledge is fundamental for the development of interventions and health care on equal terms. Caregivers are supposed to utilize knowledge based on evidence, however this evidence is sometimes based on groups not equivalent to the caretaker. Rafnsson et al stress that reliable data on differences by ethnicity are important to providing clues to disease aetiology and for evidence-based public health policies, for example intervention. The lack of ethnically relevant data on cardiovascular disease and diabetes across the EU leads to a weak base for health care interventions for migrant and ethnic minority populations [4].

The immigrants in Sweden belong to more than hundred different nationalities, speaking equally many languages. Although immigrants are a heterogeneous group, exhibiting significant ethnic group differences in, for example, self-reported health, many previous immigration studies in Sweden have been performed on unspecified populations of immigrants. We risk underestimating any possible differences in life quality and health status correlated to groups of different origin, if we view immigrants as one group. Studies in Sweden should therefore ideally be performed, among immigrants of homogenous ethnicity, with the same language, geographical origin, religion or cultural distance from Sweden [5, 6].

1.1 DIABETES

1.1.1 Definition and classification of Diabetes Mellitus

Historical records have shown that diabetes was diagnosed as early as 1000 years BC, and the sweet taste of glucosuria led to the diagnose diabetes mellitus which roughly means large volume of passing urine (diabetes) and sweet as honey (mellitus) [7].

Diabetes is defined by the American Diabetes Association (ADA) as a group of metabolic diseases characterized by high blood glucose levels, hyperglycaemia, as a result from impaired insulin secretion, defect insulin action, or both. The development of diabetes involve several pathogenic processes, from autoimmune destruction of the pancreatic b-cells, with consequent insulin deficiency, to different types of abnormalities that result in resistance to insulin action. Thus the developed diabetes fall into two etiopathogenetic categories, type 1 diabetes and type 2 diabetes, respectively [2].

Type 1 diabetes or immune-mediated diabetes, previously known as insulin-dependent diabetes or juvenile-onset diabetes, accounts for only 5–10% of those with diabetes (10–15% in Sweden) [8] and onset is usually early in life, however it can occur at any age for example latent autoimmune diabetes in adults (LADA) where, despite the presence of islet antibodies, progression of autoimmune β -cell failure is slow [9].

The cause in type 1 diabetes is a deficiency of insulin secretion due to cellular-mediated autoimmune destruction of the β -cells of the pancreas. Several markers of the immune destruction are involved, for example islet cell autoantibodies, autoantibodies to insulin, autoantibodies to Glutamic Acid Decarboxylase GAD (GAD65), and autoantibodies to the tyrosine phosphatases IA-2 and IA-2b. This autoimmune destruction has multiple genetic predispositions however there are also contributing environmental factors that are still poorly understood. Obesity is rarely observed in patients when diagnosed with this type of diabetes, however the presence of obesity is not incompatible with the diagnosis. Although autoantibodies are present in most individuals (85–90%) when diagnosed with type 1 diabetes, GAD autoantibodies can also be found in patients without diabetes [2, 7, 10].

Type 2 diabetes, previously known as non-insulin-dependent or adult onset diabetes accounts for 90–95% of those with diabetes (85–90% in Sweden) [8], and is thus a much more prevalent category with many different causes and unknown specific etiologies. Older people, people with obesity, lack of physical activity, hypertension and/or dyslipidaemia and women with prior gestational diabetes mellitus (GDM) have a higher risk of developing this form of diabetes. Some racial/ethnic subgroups also have a higher risk and this is often associated with a strong complex and not clearly understood genetic predisposition.

In this form of diabetes, autoimmune destruction of β -cells does not occur, however there is a resistance to insulin action and usually there is relative insulin deficiency. This leads to a degree of hyperglycaemia sufficient to cause pathologic and functional changes in various target tissues. Hyperglycaemia may be present for a long period of time before diabetes is detected because the hyperglycaemia develops gradually and at earlier stages it does not cause overt symptoms of diabetes and is therefore often missed. During this asymptomatic period, the abnormality in carbohydrate metabolism can cause both impaired fasting glucose (IFG) as well as impaired glucose tolerance (IGT), without fulfilling the diagnostic criteria for diabetes.

Insulin levels can be normal or elevated in response to hyperglycaemia, but this insulin secretion is defective and insufficient to compensate for insulin resistance.

The disease may change over time, depending on the severity of the metabolic abnormality, and can progress, regress, or remain stationary, depending on the extent of the underlying disease process and treatment for example with exercise, weight reduction and/or oral glucose-lowering agents. Whether insulin treatment is necessary or not depends on the extent of β -cell destruction. Some individuals can survive without insulin and some require insulin for lifetime.

Most patients with type 2 diabetes are overweight or obese. Excess weight itself causes some degree of insulin resistance, which can be reversed with weight reduction and/or pharmacological treatment of hyperglycaemia but is seldom restored to normal. Although obesity is a significant contributor to type 2 diabetes, patients with normal weight criteria may also develop type 2 diabetes depending on an increased percentage of body fat distributed predominantly in the abdominal region, central obesity. Ketoacidosis, which is more common in type 1 diabetes, seldom occurs spontaneously in type 2 diabetes. If ketoacidosis occurs it is usually in association with the stress of another illness such as infection [2, 7, 10].

Gestational diabetes mellitus (GDM)

In a normal pregnancy, there is an insulin resistance and hyper-insulinemia, due to hormonal changes. This ensures that the foetus has an ample supply of fuel and nutrients at all times. If the pancreatic function is not sufficient to secrete adequate amounts of additional insulin to overcome the insulin resistance, GDM develops with increased risks of preeclampsia, macrosomia, necessity for caesarean delivery, and their associated morbidities.

GDM is defined as any degree of glucose intolerance with onset or first recognized during pregnancy. Although there is a risk for future overt diabetes most cases resolve after delivery. There is also an increase of undiagnosed type 2 diabetes in women of childbearing age due to the on-going epidemic of obesity and diabetes, which has led to more type 2 diabetes being diagnosed in pregnancy check-ups [11].

Approximately 7% of all pregnancies (ranging from 1 to 14%, depending on the population studied and the diagnostic tests employed) are complicated by GDM[12].

Other specific types (causes) of diabetes: These types are rare and will only briefly be reviewed.

Maturity onset diabetes of the young (MODY) is characterized by impaired insulin secretion with minimal or no defects in insulin action.

Diseases such as pancreatitis, cystic fibrosis, infection (viruses) and pancreatic carcinoma, or injury from trauma for example pancreatectomy of the exocrine pancreas, can damage β -cells and cause diabetes. Tumours (somatostatinomas, aldosteronomas) and chemicals/drugs like Vacor (a rat-poison), pentamidine, nicotinic acid, glucocorticoids, thyroid hormone, diazoxide, β -adrenergic-agonists, thiazides, interferon and certain anti-psychotic drugs can by inhibiting insulin secretion cause diabetes. There can be defects in insulin action for example 1) genetic abnormalities like inability to convert pro-insulin to insulin, impaired insulin-receptor binding or production of mutant insulin molecules, 2) mutations of the insulin receptor and 3) insulin antagonizers (hormones such as growth hormone, cortisol, glucagon, epinephrine) or anti-insulin receptor antibodies[2, 7, 10].

1.1.2 Diabetes Symptoms and Complications

Diabetes symptoms, especially if marked hyperglycaemia, include thirst, polydipsia, polyuria, weight loss, sometimes with polyphagia, and blurred vision. Life-threatening consequences of uncontrolled diabetes are ketoacidosis or the non-ketotic hyperosmolar syndrome. Chronic hyperglycaemia is associated with long-term damage, dysfunction, and failure of different organs, especially the eyes, kidneys and nerves, leading to potential loss of vision, renal failure and neural dysfunction. The combination peripheral sensory neuropathy and angiopathy increases the risk of foot ulcers and eventually amputations. Especially in type 2 diabetes hypertension and abnormalities of lipoprotein metabolism are often found which in its turn affect blood vessels leading to an increased incidence of atherosclerotic, cardiovascular, peripheral arterial, and cerebrovascular disease. Chronic hyperglycaemia can also lead to impairment of growth and susceptibility to infections [2, 7, 10].

1.1.3 Diabetes Prevalence

According to the International Diabetes Federation (IDF), more than 366 million people 20-79 years of age had diabetes in 2011, which equals a global prevalence of 8.3%. By 2030 this number is estimated to rise to 552 million and the prevalence to 9.9%. The number of people with type 2 diabetes is increasing in every country and 80% of people with diabetes live in low- and middle-income countries. Approximately 50% are undiagnosed and most people with diabetes are between 40 to 59 years of age.

Furthermore, IDF has reported a 6.4% prevalence of IGT globally, corresponding to 280 millions of people in 2011. By 2030 the number of people with IGT is expected to rise to 398 millions with a prevalence of 7.1%.

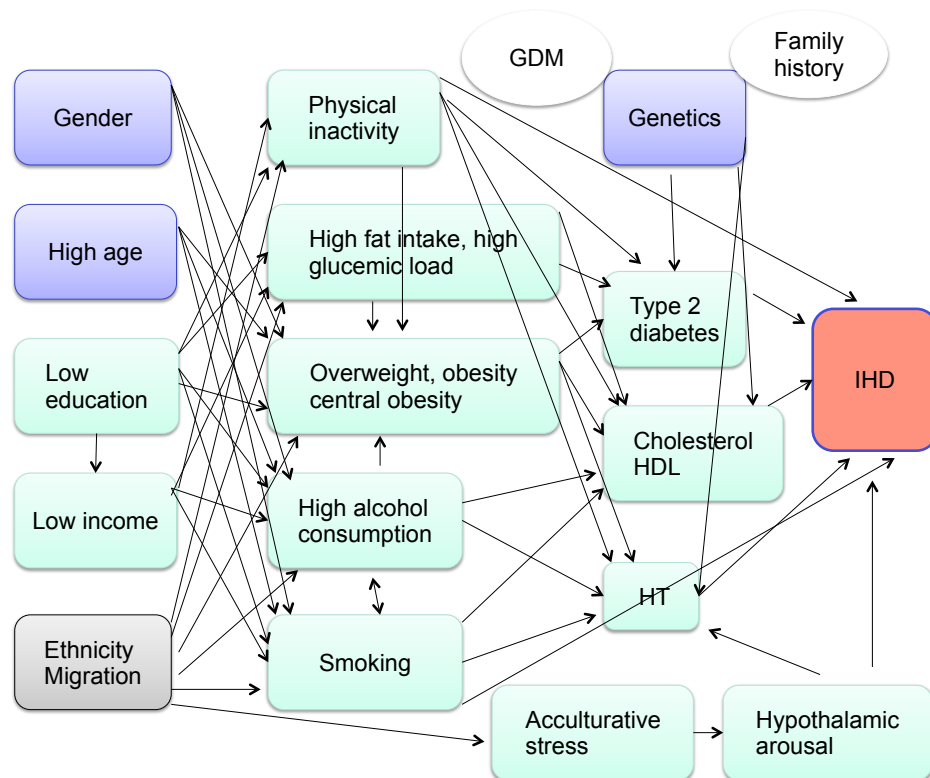
1.1.4 Risk factors for diabetes

High blood pressure, tobacco use, high blood glucose, physical inactivity, overweight and obesity, are associated with increasing risks of chronic non- communicable diseases such as heart disease, diabetes and cancers and are the leading global risk factors for mortality in all income groups worldwide [13].

In a study by Bonora et al. the incidence rates for diabetes were elevated 11-fold in individuals with IFG, 10-fold in individuals with obesity, 4-fold in those with IGT, 3-fold in those with overweight and 2-fold in those with dyslipidaemia or hypertension [14].

For intervention and prevention of disease and injury, it is of outmost importance to identify the health risks that underlie these risk factors as well as the background causes. This is a complex causal chain, consisting of socioeconomic factors, environmental and community conditions, as well as individual life-style behaviour (Figure 1).

Figure 1 – (Non-exhaustive) Illustration of the “causal-chain” of pathways to Ischaemic Heart Disease (IHD) passing type 2 diabetes.



HDL: High density lipoprotein HT: Hypertension. Green are modifiable risk-factors, blue are non-modifiable risk-factors. (Based on the WHO 2009: Data Global health risks: mortality and burden of disease attributable to selected major risks. 1. Risk factors).

Risk factors and associated disorders for diabetes have according to IDF been described as modifiable and non-modifiable[15]. Although some risk factors listed below are not studied in this thesis, they are described because they are considered in the discussion.

1.1.5 Modifiable risk factors

1.1.5.1 Overweight, Obesity and Central Obesity.

The worldwide prevalence of obesity was 35% in adults year 2008, (nearly doubled compared to 1980) [16]. Type 2 diabetes is caused by a combination of genetic and life-style factors, however obesity is a powerful predictor of, and the most important single risk factor for Type 2 diabetes. The collected evidence for the association of overweight and obesity (central and total) with diabetes is overwhelming [12, 17, 18]. A study in Sweden on middle-aged men showed approximately the same odds for diabetes if the men had obesity without the metabolic syndrome (OR: 3.49) as if they had the metabolic syndrome without obesity (OR: 3.28), however odds increased to 7.77 if having both [19]. Intervention regarding obesity has been shown to decrease the incidence of Type 2 diabetes. Although obesity is significant, central obesity reflecting the abdominal fat may be an even better indicator of the risk of type 2 diabetes [20-23].

Diagnostic criteria for Overweight, Obesity and Central Obesity are shown in Table 1. These criteria are based on risks for diabetes, however a study in Canada from 2011 has

shown cut-off values at 24 kg/ m² in South Asian, 25 kg/ m² in Chinese and 26 kg/ m² in black people when comparing to diabetes risk in Europeans at 30 kg/m². This indicates that cut-off values need to be tailored to lower the risks [24].

Table 1 – Data based on WHO criteria. Ethnicity should be the basis for classification, not the country of residence. *In the USA the Adult Treatment Panel III values (102 cm male; 88 cm female) are likely to continue to be used for clinical purposes.

Overweight	BMI ≥ 25 kg/ m ² . For people of Asian descent BMI ≥ 23 kg/ m ² .		
Obesity	BMI ≥ 30 kg/ m ² . For people of Asian descent BMI ≥ 27.5 kg/ m ² .		
Central Obesity	Europeans*	Male ≥94cm	Female ≥80cm
	South Asians	Male ≥90cm	Female ≥80cm
	Chinese	Male ≥90cm	Female ≥80cm
	Japanese	Male ≥90cm	Female ≥80cm
	Ethnic South and Central Americans:	Use South Asian Recommendations until more specific data are available.	
	Sub-Saharan Africans:	Use European data until more specific data are available.	
	Eastern Mediterranean and Middle East:	Use European data until more specific data are available (Arab) populations.	

1.1.5.2 Sedentary lifestyle

Physical inactivity

During the last decades physical inactivity has increased in many populations, contributing to the current global rise of obesity. Many studies, cross-sectional as well as longitudinal, have shown physical inactivity to be an independent predictor of Type 2 diabetes in both men and women [25-27]. For equivalent degrees of obesity, more physically active subjects have a lower incidence of diabetes [28]. Physical activity can be measured in many different ways. The choice of method is often a compromise between accuracy level and feasibility, however it is important that the choice of tool suits the aims of the research. Self-report methods are often the least expensive, however also the least accurate [23].

Dietary factors

Some of the more consistent studies indicate that a high total calorie and low dietary fibre intake, a high glycaemic load and a low polyunsaturated to saturated fat ratio may increase the risk for diabetes [12]. The EPICOR study investigated the association of glycaemic index and glycaemic load with coronary heart disease in a large and heterogeneous cohort of Italian men and women. In this cohort, high dietary glycaemic load and carbohydrate intake from high-glycaemic index foods increased the overall risk of CHD in women but not men [29].

Smoking and alcohol consumption

These are two other important risk factors for diabetes. Moderate regular alcohol consumption has in one study showed reduced prevalence of impaired glucose tolerance and high intake of alcohol among men was in another study associated with increased risk of diabetes. A review from 2007 showed that active smoking is associated with an increased risk of type 2 diabetes [30-32].

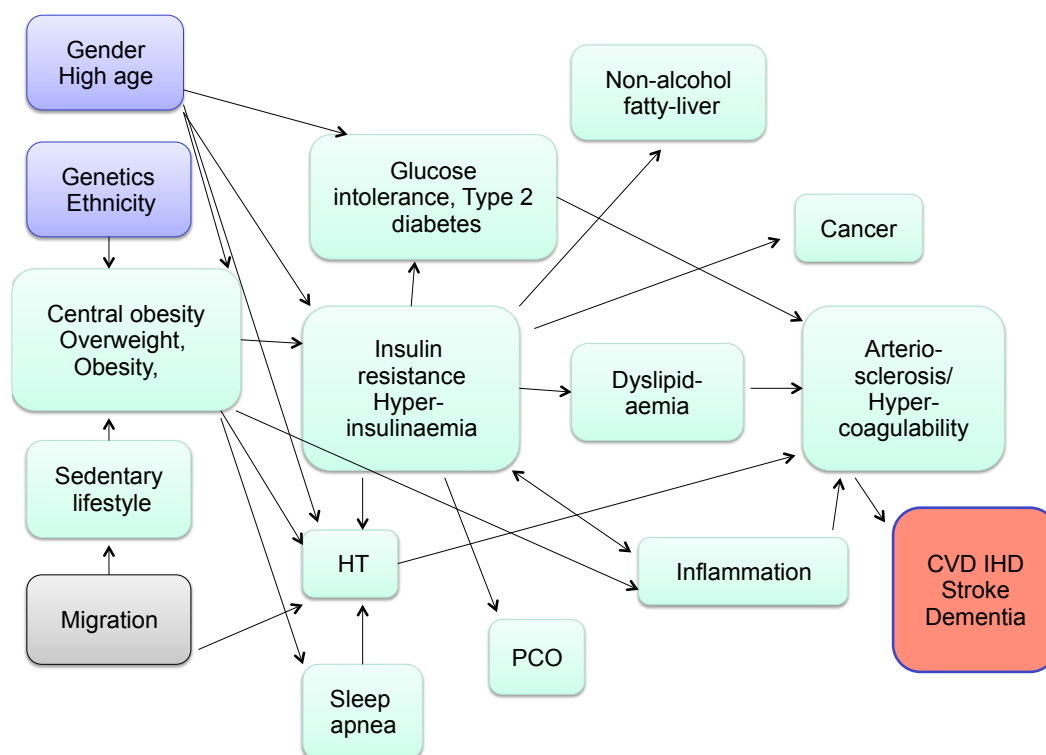
Previously identified glucose intolerance (IGT) and/or impaired fasting glucose (IFG).

IGT and IFG also called pre-diabetes are highly prevalent worldwide. It is estimated that 7.9% of the world population or 344 million people have IGT. Pre-diabetes is a metabolic state between normal glucose homeostasis and hyperglycaemia. It is a continuous pathologic process that most often starts many years before the development of abnormal glucose levels. In IGT there is an association with insulin resistance in the skeletal muscles and in IFG there is an impaired function of insulin secretion and an impaired insulin sensitivity of the liver to control hepatic glucose output. The cause of the insulin resistance is obesity and sedentary lifestyle, in combination with genetic predisposition [33]. The β -cell function will gradually decline, and by the time diabetes is clinically diagnosed around 40–70% of β -cell function has already been lost. IGT is more common than IFG and 60% of people who develop diabetes have either had IGT or IFG five years earlier. Individuals with a combined IFG and IGT have a high-risk state for diabetes, especially patients who remain with pre-diabetes despite intensive lifestyle intervention. Reversion to normal glucose regulation, even if transient, is associated with a significantly reduced risk of future diabetes [34]. Both IFG and IGT are associated with total mortality and cardiovascular risk factors, like hypertension and dyslipidaemia, with the highest risk in those with a combined IFG and IGT [33]. The Decode Study found significant increased mortality in individuals with isolated IFG (FBG 6.1–6.9mmol/l) [35]. The prevalence of IFG varies between populations and across different age groups within populations. Overall prevalence rates, in the order of 5% or more, are common and IFG is more common in men than in women [33].

1.1.5.3 The Metabolic Syndrome

The risk factors of the metabolic syndrome has been known for at least 80 years and this clustering of risk factors is also known as syndrome x, the insulin resistance syndrome and the deadly quartet. Obesity, including increased waist circumference, is at the core of the metabolic syndrome, together with high blood pressure, high triglycerides, low HDL cholesterol, and/or abnormal glucose metabolism [23]. Grouped together, these risk factors are associated with cardiovascular disease and the metabolic syndrome is considered a pre-diabetic state with a five-fold greater risk of developing type 2 diabetes [36]. In one study the odds of developing diabetes for subjects with metabolic syndrome and normal weight, metabolic syndrome with overweight, metabolic syndrome with obesity, was 3.47, 7.77, and 10.06, respectively, compared to normal weight without metabolic syndrome [19]. Just as described for diabetes, there is a causal chain for the metabolic syndrome and there are many different, yet unproven, theories of underlying mechanisms (Figure 2).

Figure 2 – (Non exhaustive) illustration of the “causal-chain” for the metabolic syndrome with some, but not all, pathways to cardiovascular disease CVD, ischemic heart disease (IHD), stroke and dementia.



Prevalence of the Metabolic Syndrome

In Europe, 20% of the adult population (without known diabetes or CVD) is affected and the prevalence is increasing among children and young adults worldwide, especially in developing countries. Of those with the metabolic syndrome approximately 50% will eventually develop type 2 diabetes [37, 38].

There are different ways to diagnose the metabolic syndrome and the criteria for diagnose are still being debated. A number of expert groups have agreed on the core components, obesity, insulin resistance, dyslipidaemia and hypertension, however the criteria to identify the components vary (Table 2). Another tool to identify metabolic syndrome features in patients with type 2 diabetes or glucose intolerance (ADA criteria) is the “Hypertriglyceridemic Waist” measurement. This tool was a significant marker of coronary artery disease at earlier age in those with glucose intolerance or type 2 diabetes [39].

Depending on which method is used, there is a variability of prevalence. The AusDiab study in Australia showed that each definition (i) World Health Organisation (WHO), (ii) European Group for Study on Insulin Resistance (EGIR) and (iii) National Cholesterol Education Program-Third Adult Treatment Panel (ATPIII) identified 15-21% as having the metabolic syndrome, however only 9.2% had criteria for all three different definitions. ATPIII definition seemed to be superior to WHO definition for predicting cardiovascular mortality and diabetes in some populations. The IDF criteria were produced with the aim of a simple diagnostic tool for use in clinical practice and research worldwide [40].

Table 2
Metabolic syndrome-definitions

	WHO (1999)	EGIR (1999)	NCEP ATPIII (2001)	AACE (2002)	IDF 2004
	Glucose intolerance, IGT or diabetes and/or insulin resistance together with two or more of the following:	Insulin resistance together with two of the following:	Three or more of the following:	The insulin resistance syndrome	
Fasting plasma glucose	Microalbuminuria	$\geq 6.1 - < 7.0$ mmol/l	≥ 5.6 mmol/l	$\geq 6.1 - < 7.0$ mmol/l + 2h-PG 7.8-11.1	≥ 5.6 mmol/l or diabetes-diagnose
Blood Pressure	$\geq 140/90$ mmHg	$\geq 140/90$ mmHg or treatment	$\geq 130/\geq 85$ mmHg	$> 130/85$ mmHg	$\geq 130/\geq 85$ mmHg or treatment
Triglycerides	≥ 1.7 mmol/l	> 2.0 mmol/l or treatment	≥ 1.7 mmol/l	≥ 1.7 mmol/l	≥ 1.7 mmol/l
HDL-cholesterol	and/or Men: < 0.9 mmol/l Women: < 1.0 mmol/l	and/or < 1.0 mmol/l or treatment	Men: < 1.03 mmol/l Women: < 1.29 mmol/l	Men: < 1.03 mmol/l Women: < 1.29 mmol/l	Men: < 1.03 mmol/l Women: < 1.29 mmol/l
Obesity	Waist-hip ratio Men > 0.90 Women > 0.85 and/or BMI > 30 kg/m ²	Waist Circumference Men: ≥ 94 cm Women: ≥ 80 cm	Waist Circumference Men: ≥ 102 cm Women: ≥ 88 cm		Waist Circumference, ethnicity-specific and any two of the above:

1.1.5.4 Dyslipidaemia

The characteristic dyslipidaemia, “the diabetic dyslipidaemia” with low HDL cholesterol, high triglycerides and increased concentration of LDL-cholesterol, is often seen in patients with type 2 diabetes [41]. With this pattern present at baseline, hazard ratio was over 2 for developing diabetes mellitus at year 5 [42]. Dyslipidaemia is not only a risk factor for diabetes, it is also one of the major risk factors for cardiovascular disease in those already diagnosed with diabetes mellitus. The prevalence of hypercholesterolemia is not necessarily higher in patients with diabetes mellitus, however mortality increases exponentially in coronary heart disease as a function of serum cholesterol levels [41].

1.1.5.5 Hypertension

Diabetes and hypertension have partly the same aetiology and disease mechanisms. Obesity, inflammation, oxidative stress, insulin resistance and mental stress are the common pathways, which influence each other eventually ending in a bad circle. Diabetes and hypertension are both considered as chronic inflammatory diseases, as end results of the metabolic syndrome and they can develop one after the other in the same individual [43]. Patients with hypertension alone have a major risk for CHD and stroke [23]. Compared to people with normal blood pressure, one study showed that those with hypertension were almost 2.5 times more likely to develop type 2 diabetes [44]. The systolic blood pressure increases with age and the lifetime prevalence of hypertension is almost 90% in populations with Western lifestyle. American studies have estimated the prevalence of hypertension in adults at around 30%. The prevalence is generally lower in women up to menopause where after levels are equal with men [45].

1.1.5.6 Low education, unemployment, deprived neighbourhood

Low educational attainment and unemployment are both associated with diabetes. In one study there was an association between diabetes and low education but not unemployment [46]. On the other hand, the DIAB-CORE study in Germany, individuals residing in neighbourhoods with high unemployment rates had elevated odds of type 2 diabetes after adjustment for age, sex, social class, and employment status [47].

1.1.6 Non-modifiable risk factors

1.1.6.1 Age

Age > 45 years is considered a risk factor. The risk of developing Type 2 diabetes increases with age, however the earlier onset has increased with increase of Type 2 diabetes among younger adults, especially in developing countries [15].

1.1.6.2 Genetics, heredity

For individuals with one parent having type 2 diabetes, the risk of developing type 2 diabetes during a lifetime is 40% (higher if the mother is affected). If both parents have type 2 diabetes the risk is 70% [17]. Although there are more than 40 genetic variants

associated with Type 2 diabetes, known genetic markers can only explain a small part of the heritage of type 2 diabetes (<15%)[48].

1.1.6.3 Previous gestational diabetes

With gestational diabetes, glucose tolerance usually returns to normal following delivery; however, these women have a substantially higher risk of developing Type 2 diabetes in later life. To have given birth to a baby weighing more than 9 pounds or 4 kilos is also considered a risk factor. In Sweden, a study on 174 women with GDM the findings were a 30% prevalence of diabetes and 51% with abnormal glucose tolerance at 5 years post partum [49].

1.1.7 Other risk factors

Inflammation

There is a link between metabolic and immune systems. The first molecular inflammatory link found was TNF- α from adipose tissue, which together with other inflammatory components like IL-1 and MCP-1 contributes significantly to insulin resistance. The C-reactive-protein is higher in people with obesity and is considered a risk marker for diabetes [50].

Intrauterine and early childhood influences may also play a role.

Include low birth-weight and exposure to a diabetic environment in utero [51, 52].

Polycystic ovarian syndrome

Polycystic ovary (PCO) syndrome is associated with subsequent incident diabetes and dyslipidaemia, independent of BMI. Diabetes risk may be greatest for women with persistent PCO symptoms [53].

Medication

Although persons with schizophrenia have increased prevalence of the metabolic syndrome due to increased prevalence of sedentary behaviour, there are data indicating that antipsychotic pharmaceuticals cause metabolic disturbances and the risk varies with different drugs [54]. Other medications associated with diabetes are steroids and hypertensive therapies like thiazide diuretics and beta-blockers [55].

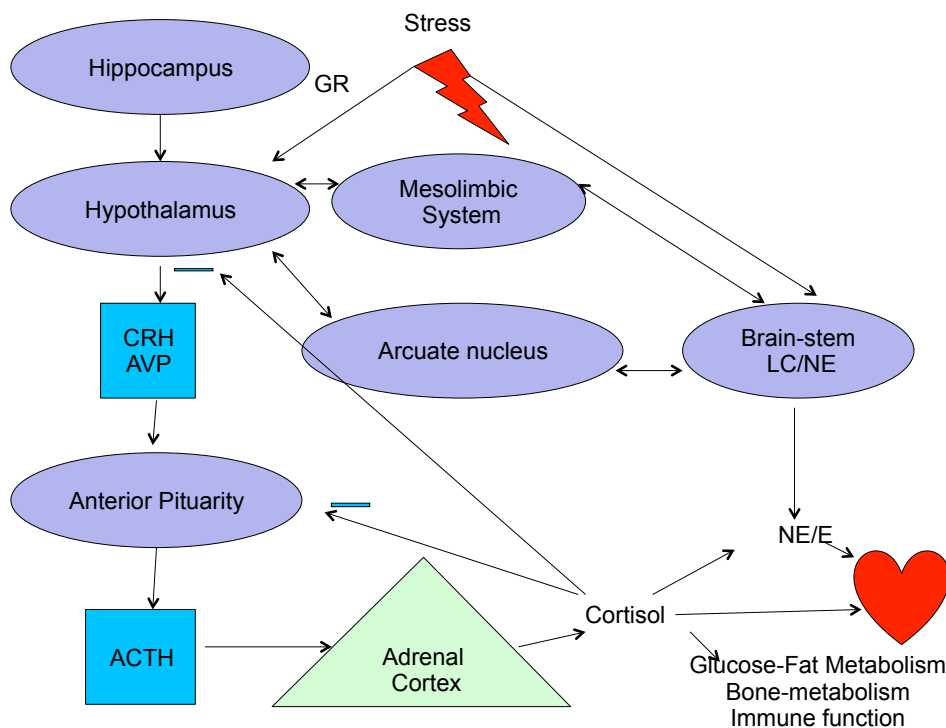
1.1.7.1 Vitamin D deficiency

There is substantial evidence supporting a relationship between vitamin D status and insulin resistance [56].

1.1.7.2 Stress

The association of clinical overt and experimental cortisol excess with metabolic disturbances has been shown in many studies. Stress causes cortisol excess and glucocorticoids are shown to cause various degrees of beta-cell dysfunction depending on the modulation of gene expression. It has been suggested that patients with the metabolic syndrome and abdominal obesity have an increased availability of glucocorticoids in the liver and the adipose tissue and the prevalence of diabetes increases according to the severity of the subclinical hypercortisolism [57]. The physiology of the stress response is illustrated in Figure 3.

Figure 3 – Schematic diagram of the hypothalamic-pituitary-adrenal (HPA) axis



CRH (corticotropin-releasing hormone) AVP (arginin-vasopressin) ACTH (adrenocorticotrophic hormone), LC (Locus ceruleus) NE (norepinephrine) E (epinephrine) GR (glucocorticoid receptor)

The main components of the stress-system are the corticotropin-releasing hormone (CRH) and the locus-ceruleus-norepinephrine (LC/NE)-autonomic systems. Activation of the system leads to changes that improve the ability for homeostasis for an increased chance of survival. The activation of the hypothalamic-pituitary-adrenal (HPA) axis leads to the production of cortisol, which has several functions. Cortisol inhibits the CRH and LC/NE systems and has insulin-mediated effects on adipose tissue, promoting visceral adiposity, insulin resistance, dyslipidemia and hypertension [58]. The physiological stress reaction aiming for homeostasis is an adaptive process known as alleostasis. If the stress is chronic or excessive the strain on the physiological system prevents a return to a healthy state of homeostasis. This strain is known as allostatic load. Stress is believed to play a major role in the development of depression with damaging effects on hippocampus (rich in glucocorticoid-receptors). This could cause a reduction in the feed-back system resulting in increased cortisol secretion “the glucocorticoid cascade hypothesis” [59]. A meta-analysis on depression for the onset of type 2 diabetes revealed a 37% increased risk of developing type 2 diabetes [60]. Other stress-related disorders like anxiety, sleeping problems and chronic pain have independently a risk of metabolic consequences. A comorbidity of depression and anxiety with a significant risk for onset of type 2 diabetes was described in one study [61]. Sleep deprivation is associated with reduced insulin sensitivity, obesity, impaired glucose tolerance and diabetes among men [62, 63]. Associations between chronic pain like fibromyalgia with obesity, the metabolic syndrome and diabetes has also been shown [64-66].

1.2 MIGRATION AND HEALTH

1.2.1 General definitions

The terminology regarding studies on migration and the relation with health is varying and not so homogenous. The most commonly used terms in the field are described below and the defined concepts are used in this thesis.

Migration: The Oxford Dictionary defines migration as movement of people to a new area or country in order to find work or better living conditions. The International Organization for Migration (IOM, 2005) defines migration as a process of moving, either across an international border, or within a state [67].

Immigration: A process by which non-nationals move into a country for the purpose of settlement. *Immigrant*: A person who comes to live permanently in a foreign country [67].

Ethnicity: The English Dictionary defines ethnicity as an ethnic quality or affiliation resulting from racial or cultural ties, and an ethnic group is a group of people of the same race or nationality who share a distinctive culture. In medical research, especially in America and to some extent in England the term “ethnic” usually refers to “minority groups,” like African-Americans, Vietnamese, or Hispanics, “a distinct collective group” of the population *within the larger society* whose culture is different from the mainstream culture. In Europe, however, ethnicity is associated with “nationhood” or “peoplehood”, not only minority groups. Anthropologic definitions are often more specific, for example; Ethnicity/ethnic group has by De Vos et al. been described as a group of people who hold onto common traditions not shared by others like religion, culture, language, a sense of historical continuity, common ancestry/place of origin and belonging [68].

Acculturation: To acculturate: to assimilate to a different culture, typically the dominant. Acculturation is the process of psychological and cultural change that results from continuous contact between two distinct cultural groups [69]. Further theories will be discussed below.

Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity [70].

Illness refers to the sociocultural context within which disease is experienced (the individual subjective dimension of ill-health and the diffuse consequences of the disease process). The patient and his/her family label, classify, and explain the sickness episode in such a way that it can be personally and socially meaningful [71].

Disease is the professional dimension of ill-health, any condition that impairs normal function [71].

1.2.2 Immigration in Sweden

Due to the globalisation process, international migration has increased to reach an estimated number of 213 million international migrants in 2010 [72].

In 2004, approximately 12 % of the population in Sweden was foreign-born. By 2012 this population had grown to 15% largely due to immigration mainly to the large cities such as Malmö, Gothenburg and Stockholm, from Iraq and later on from Syria. In year 2012, around 20% of the population in Sweden had immigrant background,

defined as persons who are foreign born or native-born with either one or two foreign-born parents.

In 2004, the Turkish immigrant group was one of the four largest. Although new large immigrant groups from Iraq and Syria are forming in Sweden, the Turkish born immigrant-group is still one of the largest with approximately 45,000 first generation immigrants and 70,000 with Turkish background [73].

1.2.2.1 Turkish migrants

With about 6% of its population abroad, Turkey is one of the worlds leading migrant-sending countries. Turkish labour emigration to Europe started in the 1960s with an agreement signed by the Turkish and West German governments. Similar agreements were signed with Sweden. The reason for the labour emigration is being debated. Some argue that high unemployment rate in Turkey led to increased migration of Turkish unskilled labour, "guest workers," from rural areas to major urban centres. The agreement was to provide the German economy with temporary workers, while thinning the ranks of Turkey's unemployed. On the other side some analysis reveal that the main reason for the agreement was for unskilled and rural people to gain skills that were needed in Turkey, not to decrease unemployment. To view Turkish migrants as "unskilled and rural who mainly originated from central and eastern Anatolia" is according to Akgündüz an imagined construction as far as the majority of migrants were concerned. Many immigrants were in fact skilled workers and the Turkish officials tried to prevent them from migrating [74, 75].

The economic downturn in Western Europe in the mid 1970s ended the recruitment of labour from Turkey, however emigration continued for other reasons such as family reunion and refugee movement in the 1980s and 1990s. A large number of family reunions were after 1980s via marriages, where immigrants already living in Europe would choose a spouse from Turkey. A new form of family reunification the "marriage migration" became after the 1980s one of the main reasons for migration to Europe. Another important reason of migration was the Kurdish minority. So the growth of the Turkish communities in Europe can be explained by several factors. First of all, many labour-immigrants did not return to their birth-country as planned, which led to family-reunions and bringing spouses from Turkey as a result. Secondly, the increased number of refugees seeking asylum contributed. Thirdly as a result of family-reunions and bringing spouses the birth rate increased and a large number of Turkish children were born in Europe. Finally, the last few years have witnessed an increase in the number of highly qualified professionals and university graduates moving to Europe or the CIS countries. Meanwhile, the number of second and third generation migrants grew and the number of people in Europe with Turkish background is approximately 3.2 million, including sizeable Turkish diaspora communities in several European countries, where Sweden is one of them [72, 74, 75].

1.2.2.2 Ethnic Turks

Turkic peoples are a collection of ethnic groups that live in northern, eastern, central and western Asia, north western China and parts of eastern Europe [76]. It is very difficult to calculate the exact number of ethnic Turks in Sweden however according to Turkish Associations in Sweden the estimation is around 15,000.

This number includes ethnic Turks from Turkey and the Balkan countries. Most of the ethnic Turks live in the south of Sweden.

People with Turkish background are normally defined as people with Turkish mother tongue however, in Sweden, registers do not take any consideration to mother tongue, only country of birth. Therefore ethnic groups with different mother tongues like the Kurdish-, Assyrian-Syrian- and Armenian-groups are included in the statistics for Turkish immigrants [5].

There are no records on the number of people with Kurdish decent in Sweden. According to Kurdish organizations, data vary between 50.000-100.000. A majority of the Kurdish population in Sweden are born in Turkey however there are also Kurds from Iraq, Iran, Lebanon and Syria living in Sweden. One of the first Kurdish groups that migrated to Sweden was from the Konya-area in central Anatolia [5].

1.2.3 Migration and acculturation

Several theories about migration have developed during history. Already in the 1880s, the geographer E.G. Ravenstein developed a series of migration 'laws'; most migration is over a short distance, occurs in steps, usually to urban areas, females are more migratory than males (who are more migratory over long distances) and most migrants are adults who mostly migrate due to economic causes. This became the basis for the modern migration theory. Migration can be voluntary or forced and two groups of factors causing migration have been described: push and pull factors. Push factors are things that are unfavourable about the area that one lives in, and pull factors are things that attract one to another area [77].

Five stages of the migration have been identified; 1) Planning, where excitement, anxiety and tension can prevail for hours to months. 2) Migration. The duration of migration could be for hours to years (especially for those living in refuge-camps). 3) Over-compensation is characterized by novelty and task-oriented adaptation which usually lasts for 6 months to one year after arrival. 4) De-compensation is characterized by acculturation (i.e. the integration into a new society) and/or cultural shock, loss, mourning. This stage usually last for 6 months to one year after arrival. 5) Resolution or stage of inter-generational support, characterized by being occupied with rearing bicultural children or establishing a personal and social network. Each of these stages is associated with stress. Although there may be positive feelings of relief there could also be negative feelings, which in turn can cause psychological and physical problems. Usually, problems that were suppressed earlier manifest themselves in stage 4 as somatic complaints [78].

There are large variations in how people acculturate and in how well they adapt to this process. Adaptation is better among persons who engage in both their heritage culture and in the larger society (integration) than those who engage only in their heritage culture (separation), only in the larger society (assimilation) or to neither culture (marginalization). A successful coping mechanism is related to both physical and mental health correlates.

A pressure to change and the experience of an unfamiliar social and physical environment can lead to *acculturative stress*. Some immigrants may not experience acculturative stress, on the contrary, many may experience an initial relief by feeling safe and being better off than the people in their home country, however the positive

effects may decrease after a period when the acculturating individual has to cope with a low socio-economic status in the new country and perhaps prejudices, xenophobia and discrimination. The most important sources of acculturative stress, however, are language competency variables [79]

1.2.4 Healthy immigrant hypothesis

This hypothesis refers to an observed phenomenon that the immigrants are healthier than the native-born residents. However, there is substantial evidence that the duration of stay in the receiving country plays an important role in the modification of health status. Initially advantageous lower overall mortality in spite of being socio-economical disadvantaged may turn into a mortality disadvantage when socio-economic conditions continue to be unfavourable and access to health care is difficult. Therefore, the healthy immigrant effect may not apply equally to all groups of immigrants [80-82].

1.2.5 Poor health among immigrants

There are several factors that contribute to poor health among immigrants. First of all, the individual lifestyle factors such as, smoking, alcohol/ drug abuse, low educational attainment, low socio-economic status, low health literacy and poor health-seeking behaviour. Secondly, social and community influences, such as separation from family, anti-migrant sentiment in the host community, poor working conditions and the lack of migrant-inclusive services. Xenophobia, social exclusion, discrimination, conflicts and political instability also add to poor health [67].

1.2.6 Self-reported health

Self-rated or self-reported health (SRH) is a powerful predictor of clinical outcome as well as of morbidity and mortality. Using one single question, the patients rate their health from excellent to very poor. SRH is one of the best predictors for cancer survival and it provides useful endpoints for clinical trials [83].

Several studies have shown that immigrants report lower SRH than non-immigrants. A study performed in Switzerland showed lower SRH among immigrants compared to a Swiss population [84]. In a report from the Swedish Survey of Living Conditions in the year 2000, four immigrant groups were studied regarding self-reported health, comparing the groups to each other and to a Swedish-born population. The rate of ill-health was larger among the immigrants and varied between the groups[5]. A further analysis of the same material showed a strong association between ethnicity and poor self-reported health that seemed to be mediated by socioeconomic status, poor acculturation, and discrimination [85].

1.2.7 Psychological distress, psychiatric illness

The increased risk of poor mental health and psychological distress among immigrants has been confirmed by several previous studies. In one study, ethnicity was the strongest risk mediator for mental illness among Latin American refugees in Sweden [86]. A low sense of coherence, poor acculturation among the men, poor sense of control, and economic difficulties in exile, seemed to be stronger risk factors for psychological distress among Iranians and Chileans than exposure to violence before

migration [87]. Another study presented higher odds for psychiatric illness and intake of psychotropic drugs among immigrants from Iran, Chile, Turkey and Poland compared to Swedish controls. When using the Polish group as controls and adjusting for sex, age, marital status, knowledge of Swedish, employment and sense of coherence, the Iranian group had higher odds for self-reported longstanding psychiatric illness underlining the impact of ethnicity. [88].

1.2.8 Pain and somatisation

Pain disorders, such as musculoskeletal pain, are one of the main reasons for long-term sick leave in Sweden. A study of musculoskeletal disease showed that the strongest independent risk indicator was being born outside Sweden, even when compared with socioeconomic class [89]. Another study concluded that immigrant patients live under more strained psychosocial conditions and experience a deeper impact of pain than the Swedish control group [90]. In Switzerland the outcome of pain disorder in patients with a history of migration was affected by the degree of inclusion in the Swiss society [91]. Somatisation (the tendency to experience and communicate psychological and social distress in the form of physical symptoms, and to seek medical help for it) has been described among immigrants. The differences in somatization between different ethno-cultural groups could be different styles of expressing distress [92]. A study in Israel showed that somatisation was a prevalent problem among immigrants from the former Soviet Union and associated with psychological distress [93].

1.2.9 Non-communicable diseases

The major cause of morbidity and mortality in industrialized countries are non-communicable diseases. In the acculturation process, immigrants who adopt the health-profile of the local population can increase their risk for CHD, cerebrovascular disease, diabetes and cancer. For example migrants with low risk of certain cancer-types could exhibit similar risk profiles as the local population [80].

1.2.9.1 Overweight, Obesity and dyslipoproteinemia among immigrants

A higher prevalence of risk factors for IHD among immigrants than the indigenous population has been described in many studies. For example immigrant women from Turkey and Iran were heavier, had a higher prevalence of central obesity, a more unfavourable lipid profile, and higher degree of physical inactivity than women born in Sweden [94]. A study on 60-year old foreign born men and women in Stockholm showed a diabetic pattern in the lipid-profile and when compared with the Swedish group there was a lower risk of high total cholesterol and LDL-cholesterol but a higher risk of low HDL-cholesterol and high triglycerides [95]. The Giessen study of Turkish immigrants in Germany showed that dyslipoproteinemia was the highest prevalence of all risk factors in both genders. Total cholesterol-levels were remarkably higher than in Turkey and comparable to those of other western countries indicating an assimilation of lipid patterns to western populations. However the reason for the low levels of HDL-cholesterol and apolipoproteins stayed unclear [96]. Increased prevalence of overweight and obesity among different immigrant groups has also been shown, for example BMI, even after adjustment for age, educational status, physical activity and smoking habits, there was a strong influence of country of birth, with

significantly higher levels of BMI among Polish and Chilean men and Chilean and Turkish women, than among their Swedish controls [97].

1.2.9.2 Hypertension differs between different populations.

High prevalence of hypertension has been reported in studies on immigrants, however a study on 60-year-old women and men in Sweden showed a lower prevalence in non-European immigrants (51% in men and 36% in women) compared to Swedish-born individuals (61% in men and 44% in women) [98]. On the other hand elderly Iranians in Sweden showed greater risks of hypertension and smoking compared with elderly Iranians in Iran, and risks were higher among immigrants in Sweden from southern Europe than in their countries of birth, which typically had low coronary heart-disease mortality [94].

1.2.9.3 Dietary changes in immigrants after migration.

One meta-analyse indicated a substantial increase in energy and fat intake (meat and dairy foods), a reduction in carbohydrates and a low intake of fibre and vegetables among South Asians [99]. Dietary changes and lack of sun-light can lead to vitamin D deficiency and a study on immigrants in Norway showed a deficiency in almost 65% of women from Pakistan [100].

1.2.9.4 The prevalence of diabetes among immigrants.

When there is major, rapid change of lifestyle, dramatic increases in Type 2 diabetes has been observed with a high prevalence in some ethnic groups as a result. The highest comparative prevalences have been found in the Western Pacific area, especially the islands (25 to 37%) followed by the Middle East-Northern Africa region (17 to 24%) Turkey had a comparative prevalence of 7,91% and Sweden 4,23% [101, 102].

Many studies confirm higher diabetes prevalence among immigrants, when compared to the indigenous population. One example is a review showing a high prevalence of type 2 diabetes among Turkish and Moroccan immigrants, when compared to the indigenous population in North West Europe [103]. In another review on immigrants in Nordic countries, excess risk was found especially in women from the Middle East [104]. When compared to a Swedish population of 60-years-olds and in a group of patients aged 35-64 years, non-European immigrants showed a three-fold higher prevalence compared to the Swedish-born [105](15). Ethnic differences in prevalence of GDM have also been shown where ethnic minorities had significant higher levels. Pre-pregnant BMI and ethnic minority origin (South Asians OR 2.54) were independent predictors, while education, body height and family history had little impact [106].

A review on migration and its impact on adiposity and type 2 diabetes, showed that the risk escalation followed a gradient as migrants became more affluent and urbanized. Contributing factors were mechanisation and changes of lifestyle [107]. While many studies have shown a higher prevalence of several non-communicable diseases and their risk factors among immigrants, there are also studies showing a higher rate of illness among immigrants than found in the country of origin, indicating migration as a risk factor [108].

In a study on immigrants from the Middle East, findings were an earlier onset, stronger family history and more rapid decline of B-cell function than the Swedish controls, suggesting a different form of type 2 diabetes than in the Swedish group [109]. The ethnic predisposition affects prevalence, onset and progression of diabetes depending on genetics, environment and lifestyle factors. Exposed to similar environments, the magnitude of the differences implies a significant genetic contribution however genes linked to this susceptibility has not yet been possible to definitely identify [110].

The prevalence of diabetes and risk factors for diabetes seems to be higher in Turkish immigrants in many countries in Europe including Sweden. What impact genetics, environment and lifestyle has on this increased risk is important to analyse. If the prevalence of diabetes among Turkish immigrants in Sweden is lower than among people in Turkey one can assume a healthy immigrant effect and if the prevalence is higher in Sweden and equal to the Swedish population one could assume adaptation and acculturation through lifestyle and environment. However if the prevalence is higher in the Turkish immigrants in Sweden than in the Swedish population in Sweden and the Turkish population in Turkey there could be some other effects than mainly lifestyle changes.

2 AIMS

2.1 GENERAL AIM:

To investigate whether the Turkish immigrant group in Sweden is a risk category concerning disturbed glucose tolerance (diabetes, impaired glucose tolerance, impaired fasting glucose) and to study possible effects of migration and diabetes associated risk factors including stress-symptoms.

2.2 SPECIFIC AIMS

2.2.1 Study I

To study whether the prevalence of self-reported diabetes, in Turkish immigrants in Sweden, was higher than in Swedish-born participants, and if found whether this could be explained by overweight/obesity and differences in socio-economic status (education and employment).

2.2.2 Study II

To study whether there was a difference in self-reported anxiety, sleeping problems and pain in Turkish-born immigrants compared with Swedish controls and whether this hypothesised difference remained after adjusting for socio-economic status (education, marital status and employment).

2.2.3 Study III

To study whether the prevalence of diabetes and impaired glucose tolerance (IGT) was higher among Turkish immigrants in Flemingsberg, Sweden (who originated mainly in Konya) when compared with a Turkish population living in Konya, Turkey.

2.2.4 Study IV

To explore, among Turkish immigrants in Flemingsberg, Sweden:

- (i) whether there were associations between diabetes or IGT with different well known risk-factors like hypertension, obesity, central obesity, high fasting triglycerides, high total cholesterol, low HDL-cholesterol, metabolic syndromes, smoking, physical inactivity and low education and
- (ii) whether there were differences between sexes.

2.2.5 Study V

To study whether stress-related factors like pain, feeling depressed-worried-tired, having sleeping-problems, reporting poor self-rated health, being non-employed, having low education, drinking alcohol and being a smoker were associated with disturbed glucose tolerance and/or the metabolic syndrome in the Turkish immigrants in Flemingsberg, Sweden.

3 METHODS

3.1 PARTICIPANTS AND DATA COLLECTION IN STUDY I AND II

This thesis is partly based on data from Swedish Survey of Living Conditions (1996) combined with the first Swedish national survey of immigrants [111].

A simple random national sample of migrants born in Turkey in the ages 27-60 was drawn from the Swedish population register. Immigrants who had lived in Sweden before 1980, or had lived abroad for many years, were excluded. The response rate was about 66%, resulting in 285 male and 241 female immigrants or refugees born in Turkey, including Kurds. The participants were interviewed face-to-face in their homes by trained interviewers from September 1996 to January 1997 by Statistics Sweden, the Swedish Government-owned statistics bureau. The interview was in Swedish, and the interviewer had a questionnaire translated into Turkish, Spanish, Farsi or Polish, only used as a support when interpretation was needed. The Turkish participants were compared with a sample of native Swedes ($n = 2,854$) of the same age, interviewed during 1996 as a part of the annual Swedish Survey of Living Conditions

3.1.1 Description of the Turkish Immigrant Group in Study I and II

Study I and II. A large proportion (59%) of the Turkish-born immigrant group living in Sweden belonged to minorities, 33% Kurds, 15% Assyrians and 11% other minorities. Approximately 58% of the studied group came from smaller cities or rural areas.

Of the 526 interviews performed, 410 interviews were in Swedish, 16 with professional interpreters, 56 with interpretation by a household member, 27 with interpretation by a child, seven with interpretation by a neighbour or friend, and nine with information about interpretation was missing [111].

3.1.2 Validation of the First Swedish National Survey of Immigrants

Based on the International Classification of Diseases (ICD)-ninth revision, common symptoms such as anxiety, sleeping problems and pain were added to the questionnaire and have been used consistently since late 80s. Re-interviews (test-retest method), resulted in kappa coefficients between 0.7 and 0.9 for educational status, indicating a high level of reliability [112].

Statistics Sweden has also carried out validation studies in which self-declared information on certain types of illnesses are checked against corresponding information from medical records where rheumatic diseases showed a 68% concurrence between self-reported lower-back ailments and medical diagnose. Self-reported muscular-skeletal symptoms were generally underestimated [113].

3.2 PARTICIPANTS AND DATA COLLECTION IN STUDY III, IV AND V

The remaining part of this thesis is based on a cross-sectional total-population survey and laboratory data comprising 238 men and women (aged ≥ 20 years) who were either born in Turkey or in Sweden with both parents born in Turkey, living in Flemingsberg, Sweden.

In Study III the Turkish immigrants were compared with controls in Turkey for Disturbed Glucose Tolerance (DGT) while study IV and V focused on risk factors including stress symptoms for DGT in the Turkish women and men in Flemingsberg.

A majority of the Turkish-born population in Flemingsberg origin in the Konya area (90%), therefore data were compared with data from the TURDEP study [114] of 1549 men and women (aged ≥ 20 years) living in the Konya area in Turkey.

With diabetes mellitus and IGT estimated at 20% in Sweden and 10% in Turkey, the number of participants needed for the study was calculated to 286 persons, for a power of 90%. Non-responding was known to be high in the studied group (40%), therefore the number of participants needed was calculated to 476. The population meeting our criteria in Flemingsberg was approximately 500, why we decided to do a total-population study.

238 (55.1%) subjects completed the laboratory and physical examination, 37.8% were men and 62.2% women.

The questionnaire was based on the questionnaire used in the TURDEP survey and complemented with questions from the Diabetes Preventive Unit, the Karolinska Institute, used in the Diabetes Preventive Project 1995 on physical activity and diet (well validated for Swedish participants). Questions on stress-related symptoms were the same questions used in the Swedish National Board of Health and Welfare Immigrant Survey 1996. The questionnaire covered social, demographic characteristics, medical history, lifestyle, and reproductive history complemented by place of birth and year of immigration to Sweden. The questionnaire was initially tested in a group of participants who were my patients since many years. Some parts of the questions seemed to be difficult to understand (mostly concerning, stress symptoms, diet and physical activity) and many questions were left unanswered. Questions on stress-symptoms were translated to Turkish and back translated, and after revision, the validity improved significantly (reliability of 80%).

The same person, with the same measurement tools, measured anthropometric measurements, as weight, height and waist-circumference. Waist circumference was measured at a level midway between the lower rib margin and iliac crest with a non-stretchable tape all around the body in horizontal position. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) was measured by manual manometer, after 5 min rest, in sitting position, two times and the average calculated. If there was more than 10 mmHG difference a third measurement was performed. After an overnight fast (12 hour), blood glucose, triglycerides, total cholesterol and HDL cholesterol was taken and an oral glucose tolerance test (OGTT) was performed where the participant, within 5 minutes, would drink a 75g anhydrous glucose dissolved in 250 ml water. Those using oral anti-diabetic medications and/or insulin were considered diabetic and underwent only fasting blood glucose (FBG) and those with a medical history of diabetes without current treatment underwent FBG and, if not considered diabetic, an OGTT was performed.

3.2.1 Blood analyses

The fasting and 2-h capillary whole blood glucose concentrations were measured using a HemoCue B-Glucose Analyser with a daily calibration system (inter-assay and intra-assay coefficient of variance (CV) were 4.4% and 4.0%). In Turkey, blood

glucose concentration was measured using Glucometer Elite; instruments were checked every morning with standard solutions and after every 20 measurements with check strips (intra-assay was 3.7%).

3.2.2 Diagnosis of diabetes, IGT and IFG in study III, VI and V

In Study III, diabetes was diagnosed using U.N. World Health Organization criteria (1998)[2] if venous FBG ≥ 6.7 or if 2-h capillary blood glucose (2 h-cBG) ≥ 11.1 , and IGT was diagnosed if 2 h-capillary BG was 7.8– 11.0 mmol/l (Table 3).

In Study IV and V the WHO (2006) [2] criteria was used and diabetes was diagnosed if venous FBG was ≥ 6.1 mmol/L or if 2hr-cBG was ≥ 11.1 mmol/L, impaired glucose tolerance (IGT) was diagnosed if 2hr-cBG was 7.8-11.0 mmol/L and impaired fasting glycaemia (IFG) was diagnosed if vFBG was ≥ 5.6 - <6.1 mmol/L and if 2hr-cBG was <7.8 mmol/L. For a translation into plasma-glucose levels (Table 3).

3.3 STUDY I AND II

3.3.1 Outcome variables

Disturbed Glucose Tolerance

Diabetes mellitus was defined as self-reported presence of diabetes. Cardiac disease and hypertension were also self-reported.

Stress Symptoms

Anxiety was defined as present or not during the interview.

Sleeping problems were defined as present or not during the last two weeks before the interview.

Severe pain (severe pain or ache in neck, shoulder, lower back and/or extremities) was defined as present or not during the interview. The original response alternatives, 1: yes, severe, 2: yes, mild, 3: no, were categorised in this study into two levels, severe or not.

3.3.2 Explanatory variables

Socio economic factors

Marital status: cohabiting or single.

Employment status was dichotomised as employed or not employed.

Educational status was divided into three categories: (1) compulsory school level, <10 years, (2) between 10 and 12 years (at least two years of high school) and (3) >12 years (three years of high school or university studies).

Life style factors

Smoking habits: never smokers or former smokers or daily smokers.

BMI: based on self-reported weight and height, was calculated as weight/ height² (kg/m²) and called BMI-units. The following categories were used, according to the WHO classification: normal < 25 BMI-units, overweight 25-30 BMI-units, and obesity > 30 BMI-units.

Physical activity comprised five categories of leisure physical activity, but was in the analysis dichotomised into: being physically inactive or occasionally active vs. regular physical activity at least once a week. *Age* at the time of interview was classified according to the following groups: 27-39, 40-49, and 50-60 years of age.

Medication

Psychoactive drugs included regular use of soporific, antidepressant and/or sedative medicine.

Analgesic drugs included regular use of analgesic medicine with or without prescription.

Acculturation

Knowledge of Swedish was divided into three categories, poor, intermediate and good.

Experience of discrimination was divided into three categories, low, middle and high.

3.4 STUDY III, IV AND V

3.4.1 Outcome variables

Study IV: *Disturbed glucose tolerance (DGT):* Known diabetes with treatment, laboratory verified diabetes and laboratory verified IGT **Study V:** Newly discovered Disturbed Glucose Tolerance (new DGT): Laboratory-verified new diabetes, laboratory-verified IGT and laboratory-verified IFG (WHO criteria 2006, Table 3).

Metabolic syndrome: APTIII, IDF criteria (Table 2).

3.4.2 Explanatory variables

Risk factors

Age: For both men and women, age was dichotomized as 20–39 years and 40–85 years.

Alcohol: Three categories (never used alcohol, current users, and former users) was dichotomized as (i) never used and (ii) current users/former users.

Smoking. Three categories (never smokers, current smokers, and former smokers) were dichotomized as (i) never smokers and (ii) smokers/former smokers.

Study IV: *Hypertension:* Known hypertension with treatment and measured hypertension (SBP ≥ 140 and/or DSP ≥ 90), *Obesity:* BMI ≥ 30 kg/m², *Central obesity:* Waist circumference ≥ 94 cm for men and ≥ 80 cm for women. According to IDF consensus the European values were used until more specific data are available (Table 1). *High Fasting Triglycerides:* ≥ 1.7 mmol/L, or specific treatment for this lipid abnormality (according to IDF consensus). *High Total Cholesterol:* >6.0 mmol/L according to the Swedish national guidelines [95]. *Low HDL cholesterol:* < 1.03 mmol/L for men and < 1.29 mmol/L for women, or specific treatment for this lipid abnormality (according to IDF consensus). *Metabolic Syndrome:* APTIII, IDF criteria (Table 2)[115, 116].

Physical Inactivity was dichotomised into two categories, inactive or not inactive.

Study V: *Self-Rated Health:* The question asked was: How would you rate your general health status? Answers were in a five-graded scale from very poor, poor, fair, good, to very good Health was dichotomized as poor if the answer was very poor or poor.

Education: Low education comprised of no education (illiterate) or knowledge in reading and writing (Koran-school for example). Middle education: Elementary School only or 2 years of high-, tray- or vocational school. High education: 3-4 years of high school or college/university-studies.

Non-employed: Subjects, who were unemployed, had early retirement or long-term illness.

Employed: Subjects who worked as an employee, worked in their own or partly owned companies, those on leave from their work for example for studies or maternity/paternity leave and those who studied.

Stress-symptoms Study V: Pain: The question asked was: During the last year did you have pain in the lower back, neck and/or shoulders?

Depression: The question asked was: During the last year did you feel downhearted, sad or depressed?

Anxiety: The question asked was: During the last year did you feel worried, nervous, or anxious?

Sleeping-problems: The question asked was: During the last year have you had sleeping-problems?

Fatigue: The question asked was: During the last year have you felt fatigue?

The answers for pain, depression, anxiety, sleeping-problems and fatigue were (a) never-seldom, (b) sometimes, (c) often-all the time and they were dichotomized to (i) never-seldom and sometimes in one group (the reference group) and (ii) often-all the time in the other group.

Table 3 – Diagnose of diabetes IGT and IFG according to WHO criteria.

	WHO criteria (1998) Blood-glucose (BG)	IDF criteria (1999) WHO criteria (2006) Blood-glucose (BG)	WHO criteria (2006) Plasma-glucose (PG)
Diabetes	FBG \geq 6.7 mmol/l or 2 h-BG \geq 11.1 mmol/l (FPG \geq 2 hr PG \geq	vFBG/cFBG \geq 6.1 mmol/L or c2hr-cBG \geq 11.1 mmol/L 2 hr-vBG \geq 10.0 mmol/l	vFPG/ cFPG \geq 7.0mmol/l or 2-h vPG* \geq 11.1mmol/l or 2-h cPG \geq 12.2 mmol/l
Impaired Glucose tolerance (IGT)	2 h-BG \geq 7.8– 11.0 mmol/l. 2 hr PG \geq	2hr-cBG 7.8-11.0 mmol/L 2hr-vBG 6.7-10.0 mmol/l	vFPG/cFPG<7.0mmol/l and 2-h vPG* 7.8 - 11.1mmol/l or 2h cPG 8.9-12.1 mmol/l
Impaired fasting Glucose (IFG)		vFBG 5.6-10.0 mmol/l cFBG 5.6-11.0 mmol/l	vFPG/cFPG 6.1- 6.9mmol/l * and (if measured) 2 h vPG<7.8mmol/l

F = fasting, B = blood, p = plasma, G = glucose, V = venous, C = capillary

* Venous plasma glucose (vPG) 2-h after ingestion of 75g oral glucose load

* If 2-h plasma glucose is not measured, status is uncertain as diabetes or IGT cannot be excluded.

3.5 STATISTICAL ANALYSIS

3.5.1 Study I Study II

Data was analysed using logistic regression [117, 118]. The results were shown as odds ratios (OR) with a 95% confidence interval (95% CI). Two main models were used, the first with adjustment for age, and the second with adjustment also for educational level, employment status, and BMI level (study I) and other explanatory variables (main effect model, study II). The fit of the models was judged by residual analysis, the Hosmer-Lemeshow goodness-of-fit test. If the p-value of the test was >0.05 , the fit was considered satisfactory. A test of interaction was performed, and we did not find any interaction of interest.

3.5.2 Study III

The Turkish immigrant populations in Flemingsberg, Sweden, were compared to the Turkish population in Konya, Turkey, using t and chi-square tests. Besides showing p-values (significant if < 0.05) the difference of means and between proportions was calculated with 95% confidence interval.

3.5.3 Study IV

Data was analysed using chi2-tests and calculated by logistic regression. The results were shown as odds ratios (OR) with a 95% confidence interval (CI). There was an age-adjusted model and a full model adjusted for the other explanatory variables where the fit of the model by a goodness-of-fit test was performed. The p-value of this test was 0.95 for women and 0.82 for men, which was considered satisfactory (>0.05).

3.5.4 Study V

The data were analysed using logistic regression. The results were shown as odds ratios (OR) with 95% confidence intervals (CI). Two models were created: one comparing men and women and one age-adjusted model showing the odds for DGT and the Metabolic Syndrome for the tested explanatory variables. P-value of the goodness-of-fit test was >0.05 , thus considered satisfactory.

All statistical analyses were performed using STATA 9 or 10 by Windows

3.6 ETHICAL APPROVAL

All studies were approved by the local Ethical Committee at Karolinska Institutet

4 RESULTS

4.1 STUDY I, II

4.1.1 Study 1

The crude data showed that compared to Swedish men, Turkish men reported a lower educational level, a lower rate of hypertension and employment. Smoking and no regular physical activity were more common in Turkish men. Among Turkish women, educational level was much lower, rate of employment and hypertension lower, and overweight, obesity as well as no regular physical activity was more common than in Swedish women.

The prevalence (in the Turkish and Swedish group) of self-reported diabetes increased by age and by BMI level and decreased by educational level and employment.

Among Turkish men, age-adjusted diabetes prevalence was not higher than among Swedish men according to logistic regression, OR 1.04 (95% CI 0.35-3.11). When also adjusting for education, employment status and BMI-level, the OR was lowered to 0.89 (95% CI 0.28-2.85), however still not significant. Among Turkish women, age-adjusted diabetes prevalence was higher than among Swedish women, OR 3.22 (95% CI 1.36-7.64), however this difference was not seen after adjustment for educational level, employment status and BMI: OR was 1.22 (95% CI 0.41-3.66).

4.1.2 Study II

The crude prevalence of anxiety, sleeping-problems and severe pain as well as regular use of psychoactive and analgesic drugs was higher among the Turkish men and women when compared to the Swedish controls. The higher prevalence among the Turkish-born immigrants, showed a proportional increase between illness and medical use.

Turkish women reported a lower knowledge in Swedish compared to the Turkish men who in their turn reported more discrimination than the women. Among Turkish women there was an increasing prevalence of severe pain ($p=0.01$) with decreasing knowledge in Swedish, and increasing prevalence of anxiety ($p=0.01$) with increasing experience of discrimination. Among the Turkish men these associations were not significant. After adjustment for education, marital status and employment, Turkish men with poor knowledge in Swedish had increased odds for anxiety (OR 2.72 CI 1-01-7.38), and Turkish women with mid and high level experience of discrimination, had increased odds (OR 2.19, CI 1.06-4.54 and OR 2.58 CI 1.23-5.40, respectively) for anxiety. Finally in a full model (after adjustment for age, education, marital status and employment), being Turkish-born showed an odds ratio of around 2 for anxiety, sleeping problems and severe pain for men and an odds ratio between 2 and 3 for anxiety, sleeping problems and severe pain for women, using Swedish men and women as reference.

4.1.3 Analysis of non-response study I and II

The non-response rate was 34.4% for Turkish-born immigrants. About half of all non-respondents refused to participate. The other half could not be located, one possible

reason being repatriation without informing the Swedish authorities (i.e. the population registry) of their departure. The age distribution among respondents and non-respondents was about the same. Non-respondents were more prevalent in large cities such as Stockholm and Gothenburg, and had lower income than respondents.

4.2 STUDY III, IV AND V

4.2.1 Study III

There was no significant age difference between, the Turkish participants in Flemingsberg, Sweden, (Swedish group) and the Turkish participants in the TURDEP study in Konya, Turkey, (Turkish group). In the Swedish group, 2 h-BG, height and weight was significantly higher for both men and women, as was BMI among men, however there was no significant difference in waist-hip-ratio (WHR) between the two groups. The overall prevalence of self-reported heredity (first-degree relatives with diabetes) was 36% in the Swedish group (60% among those with diabetes, 33% among those with IGT and 31% among those with no diabetes or IGT), significantly higher than in the Turkish group who had 24%. Total amount of diabetes (those with known diabetes and new laboratory-verified diabetes), and IGT was significantly higher in the Swedish group (11.8% vs. 7.1% and 15.6% vs. 7.6%). The total amount of diabetes was significantly higher among women in the Swedish group (12.8% vs. 7.6%), and IGT was significantly higher among men in the Swedish group (17.8% vs. 4.9%). The prevalence of risk factors, like hypertension (HT), obesity, and central obesity, were similar except for a higher HT rate among Turkish women in Turkey (38.1% vs. 26.4%). Although the rate of HT was higher among the women in Turkey, mean value of SBP was higher among both men ($p < 0.001$) and women ($p = 0.020$) in the Swedish group. Crude-prevalence data are shown in Table 4.

4.2.2 Study IV

Results showed that the prevalence of diabetes or IGT increased with increasing BMI and with age (except for IGT in the oldest group). The mean age for onset of diabetes was at 47.4 years for men and at 46.2 years for women. Onset for IGT was at 47.7 years for men and at 44.7 years for women and onset for IFG was at 47.8 years for men and 38.1 for women. No significant differences between men and women concerning onset was found.

The total crude prevalence (%) of diabetes, impaired glucose tolerance (IGT) and impaired fasting glucose (IFG) in the different age-categories is illustrated in Figure 4 and age at onset of diabetes, IGT and IFG is illustrated in Figure 5.

With WHO criteria 2006 (Table 3), the crude diabetes prevalence was 16.8% and the IGT prevalence was 13.0% with a trend towards higher prevalence of diabetes among the women and IGT among the men however not significant. Before OGTT, IFG was 10.9%. After OGTT, 38% of IFG became IGT leaving an isolated IFG prevalence of 6.7% (and 4.2% with both IFG and IGT). Hypertension which had a prevalence of 30.3% in the total study population, had a trend towards higher prevalence among men than women and this difference was not significant, however prevalence of obesity was significantly higher in women, 35.1% (18.9% in men), who also had significantly higher low-HDL-cholesterol, 38.8% (23.6% in men). Central

obesity was 50% in the total study population with a non-significant trend toward higher prevalence among women. The total prevalence of the metabolic syndrome was according to IDF criteria, 28.2%, and when measured according to APTIII criteria, the metabolic syndrome was lower, 23.1%. Women reported significantly higher prevalence of never smoking than men (54.0% vs. 36.7%), and they also reported significantly higher prevalence of physical inactivity than men (60.8% vs. 36.7%). Women also reported lower education than men (68.9% vs. 57.8%).

The crude odds for having diabetes or IGT was 2-5 times higher among those with hypertension, obesity, central obesity, high fasting triglycerides and high cholesterol. After adjusting for age the odds decreased but remained significant except for high cholesterol. Low HDL-cholesterol showed 2 times higher odds for having diabetes after adjustment for age. Of those with metabolic syndrome the odds for having diabetes or IGT was 13 times higher and 10 times higher after adjustment for age. Physical inactivity did not show significant odds for diabetes or IGT, nor did smoking/former smoking or low education after adjustment for age.

Men (Table 4) with hypertension had 4 times higher odds for DGT, however, odds were reduced to 3 after adjustment for age. Central obesity showed 3 times higher odds for DGT, however odds became non-significant after adjustment for age. The odds for DGT were 3-4 times higher for those with metabolic syndrome (IDF criteria) and smokers/former smokers. Odds diminished slightly after age adjustments. Obesity, high fasting triglycerides, high total cholesterol and physical inactivity did not show significant odds for DGT.

For women (Table 4) the odds for DGT were 3-8 times higher if having hypertension, obesity, central obesity or high fasting cholesterol. After adjustment for age, obesity, central obesity and high fasting triglycerides remained significant. The metabolic syndrome had very high odds for DGT (around 21) however, low HDL-cholesterol, smoking/former smoking, physical inactivity and low education (after adjusting for age) did not show any significant associations for DGT.

Table 5 shows a full model where hypertension and smoking, independently, showed 4-5 times higher odds for DGT among men and central obesity, and high fasting triglycerides, independently showed 4.5 times higher odds for DGT among women. Age groups were dichotomized into 19-39 years and 40-85 years. The reason for this was increased prevalence for diabetes and IGT at around 40 years.

4.2.3 Study V

Women had two times higher odds for pain, anxiety, sleeping problems and fatigue compared to men and three times higher odds for reporting poor health. Women also had six times higher odds for low education and three times higher odds for non-employment. In contrast, the odds for having employment, drinking alcohol and smoking were lower for women when compared with men.

In Table 6 the age adjusted odds for having DGT or the metabolic syndrome are shown for those showing symptoms of stress (pain, depression, anxiety, sleeping-problems and fatigue), for alcohol users and smokers, high, middle and low education and for non-employed/employed. For men the odds for DGT was four times higher if being a former or present alcohol user and former or present smoker. Having a middle-level of education showed almost four times higher odds for DGT among the men.

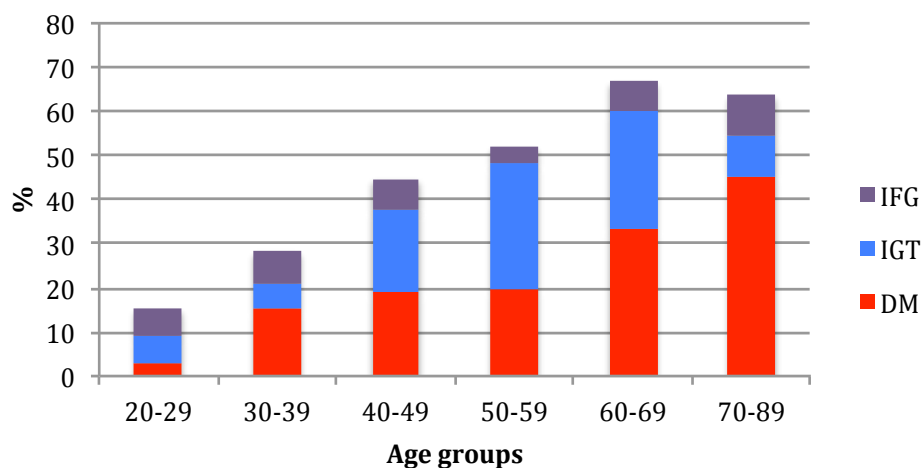
Also among the women there was an association between DGT and being a former or present alcohol user and former or present smoker. Being employed showed almost three times higher odds for DGT among the women.

We could not find any associations between the metabolic syndrome and symptoms of stress (pain, depression, anxiety, sleeping-problems and fatigue) among the men, however among the women we found lower odds for the metabolic syndrome if self-reported being depressed/downhearted/sad. The odds for self-reported poor health were not higher in the groups with DGT or the Metabolic Syndrome. Even when adding the symptoms of stress where those having all five (pain, depression, anxiety, sleeping-problems and fatigue) had the highest point (six), those who had four of five had five points and those who had three of five had four points etcetera, there was no association for trend found with DGT ($p=0.52$) nor the metabolic syndrome ($p=0.29$).

4.2.4 Non-response study II, IV and V

Of the 128 non-respondents, 38% were women and 62% men (the opposite trend to that for the participants), and the average age was 36.1 years (standard deviation 12.9) (37.6 (12.0) among men, 33.7 (13.8) among women). The non-respondents were on average significantly younger than the study participants ($p = 0.0031$). In all, 10 non-respondents (5 women and 5 men) reported diabetes (7.8%), and 32 (25.0%) reported first-degree relatives with diabetes. After adjusting for the age difference between non-respondents and respondents, we found no differences in the odds of self-reported diabetes ($OR = 1.19$; $p = 0.69$) or self-reported family history of diabetes ($p = 0.13$). Reasons for not participating were no knowledge about the study, lack of time, difficulties in taking time off work, lack of interest in participating, and “no particular reason”. For the non-respondents with diabetes, the most common reason for not participating was that they were registered with other health care units. During the survey period (year 2002-2004), 6 men died (aged 36-56) in cardiovascular events and therefore did not start or complete the survey.

Figure 4 – Total crude prevalence (%) of diabetes (DM), impaired glucose tolerance (IGT) and impaired fasting glucose (IFG) in the different age-categories among Turkish immigrants in Flemingsberg.



Number of persons in age category 20-29: 65, age category 30-39: 53, age category 40-49: 69, age category 50-59: 25, age category 60-69: 15, age category 70-89: 11, n= 238.

Figure 5 – Age at onset of diabetes (DM) impaired glucose tolerance (IGT) and impaired fasting glucose (IFG) in men and women among Turkish immigrants in Flemingsberg.

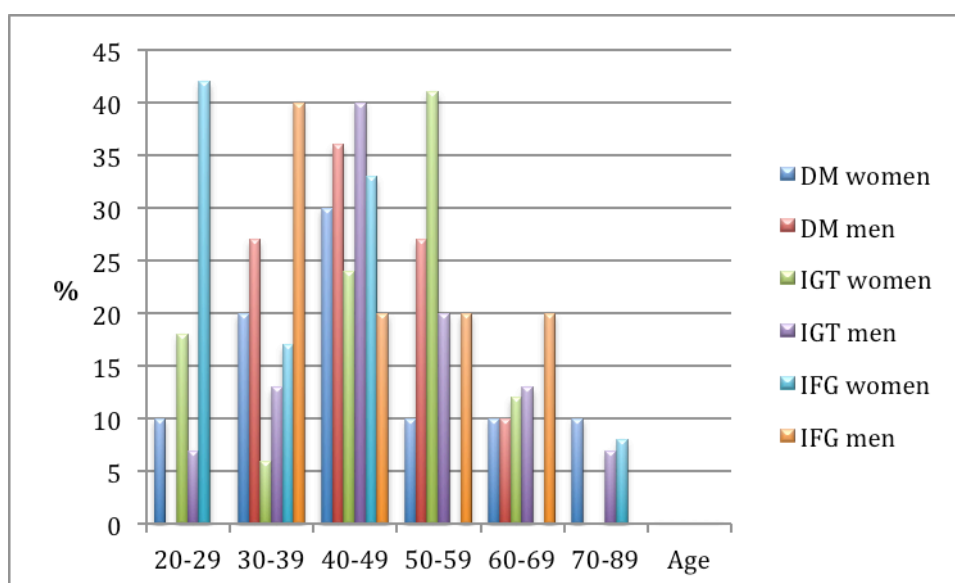


Table 4 – Prevalence of diabetes, impaired glucose tolerance, hypertension, obesity, and central obesity among first- and second-generation Turkish immigrants in Flemingsberg, and Turkish people in Konya, Turkey (crude data).

N	Turkish immigrants in Flemingsberg, Sweden N = 238 Men 90 (37.8%) Women 148 (62.2%)	Turkish people in Konya, Turkey N = 1549 Men 653 (42.2%) Women 896 (57.8%)	95% CI for difference between proportions	p value (X2 test)
Self-reported/ known diabetes	9.2% (22)	5.1% (79)	0.9–7.4%	0.010
Men	6.7% (6)	4.6% (30)	-2.8–7.0%	0.391
Women	10.8% (16)	5.5% (49)	1.0–9.7%	0.013
Self-reported heredity for diabetes (Family history of diabetes)	35.7% (85)	23.6% (366)	5.2–18.9%	<0.001
New diabetes	2.5% (6)	2.0% (31)	-1.4–2.5%	0.622
Men	3.3% (3)	1.8% (12)	-1.6–4.6%	0.411
Women	2.0% (3)	2.1% (19)	-2.6–2.4%	1.000
Laboratory verified diabetes (total: under treatment and FBG and/or OGTT verified)	11.8% (28)	7.1% (110)	0.9–8.5%	0.018
Men	10.0% (9)	6.4% (42)	-2.2–9.3%	0.262
Women	12.8% (19)	7.6% (68)	0.2–10.3%	0.037
IGT (OGTT) ^a	15.6% (37)	7.6% (118)	4.0–12.0%	<0.001
Men	17.8% (16)	4.9% (32)	7.3–18.5%	<0.001
Women	14.2% (21)	9.6% (86)	1.0–10.2%	0.106
HT ^b	30.3% (72)	35.5% (550)	-13.3–28.0%	0.113
Men	36.2% (33)	32.0% (209)	-8.0–17.2%	0.376
Women	26.4% (39)	38.1% (341)	-22.2–(-1.2)%	0.006
Obesity ^c	28.4% (67)	26.5% (410)	-5.2–9.0%	0.534
Men	18.9% (17)	14.1% (92)	-3.6–13.2%	0.228
Women	34.2% (50) ^d	35.5% (318)	-11.6–9.1%	0.770
Central obesity ^e	34.3% (81)	37.1% (574)	-11.0–5.6%	0.417
Men	23.3% (21)	21.9% (143)	-8.9–11.8%	0.758
Women	41.1% (60) ^d	48.1% (431)	-19.0–5.0%	0.116

Bold numbers: p<0.05 level. ^aImpaired glucose tolerance (oral glucose tolerance test).

^bHypertension defined as systolic blood pressure \geq 140 mmHg and/or diastolic blood pressure \geq 90 mmHg plus hypertension under treatment. ^cObesity is defined by a body mass index \geq 30 kg/m². ^dThe amount here was 146 (2 women were pregnant). ^eCentral obesity is defined by a waist measurement of \geq 102 cm for males and \geq 88 cm for females.

Table 5 – Odds ratios (OR) with 95 % confidence interval (CI) for having Disturbed Glucose Tolerance, DGT (diabetes or impaired glucose tolerance), for several risk factors (hypertension, obesity etc.) among Turkish immigrants in Flemingsberg. OR after age adjustment (Age adj.)

Ref 0 DGT=1	DGT Men OR (95% CI)	Age adj OR (95% CI)	DGT Women OR (95% CI)	Age adj OR (95% CI)
Hypertension	4.42 (1.68-11.62)	3.03 (1.07-8.58)	4.36 (2.00-9.51)	2.24 (0.90-5.58)
Obesity	1.99 (0.66-5.97)	1.64 (0.51-5.24)	5.02 (2.36-10.68)	4.03 (1.82-8.93)
Central Obesity	2.66 (1.04-6.81)	1.85 (0.68-5.05)	7.80 (3.18-19.15)	5.07 (1.95-13.16)
High fasting TG	1.47 (0.57-3.75)	1.20 (0.44-3.22)	6.43 (2.84-14.54)	5.23 (2.20-12.40)
High tot cholesterol	1.24 (0.29-5.38)	1.20 (0.26-5.44)	3.22 (1.33-7.78)	2.27 (0.87-5.91)
Low HDL- cholesterol	0.96 (0.33-2.83)	0.82 (0.27-2.56)	1.80 (0.88-3.71)	2.00 (0.91-4.42)
Metabolic Syndrome IDF	5.06 (1.87-13.66)	3.78 (1.34-10.68)	28.15 (10.86-72.97)	21.37 (7.90-57.75)
Smoking, former smoking	4.56 (1.41-14.74)	3.45 (1.02-11.63)	0.85 (0.42-1.74)	1.01 (0.47-2.16)
Physical inactivity	1.11 (0.43-2.85)	0.87 (0.32-2.40)	1.19 (0.57-2.46)	0.70 (0.31-1.58)
Education low	1.99 (0.76-5.22)	1.31 (0.46-3.72)	3.96 (1.53-10.21)	1.99 (0.70-5.66)

Table 6 – Odds ratios (OR) with 95 % confidence interval (CI) among Turkish immigrants in Flemingsberg for having DGT (diabetes or impaired glucose tolerance), for several risk factors: Hypertension (HT), Central obesity (CeOb), High fasting TG and Smoking, in men and Central Obesity (CeOb) and High fasting TG in women.

Ref 0 DGT=1	Men DGT OR (95% CI)	P	Ref 0 DGT=1	Women DGT OR (95 % CI)	P
HT	3.60 (1.23-10.53)	0.020	CeOb	4.55 (1.68-12.31)	0.003
CeOb	3.10 (0.97-9.88)	0.055	High fB-TG	4.55 (1.85-11.18)	0.001
Smoking	5.76 (1.41-23.57)	0.015	Age group	2.34 (0.95-5.84)	0.068
Age group	1.68 (0.50-5.61)	0.402			

Age group = 20-39 and 40-85 years. Full model. Goodness of fit test: 0.82 for men and 0.95 for women. Adjustment for education did not improve the model.

Table 7 – Age adjusted Odds Ratios (OR) with 95% Confidence Interval (CI) for difference between men and women in DGT and metabolic syndrome. Study population: Turkish immigrants in Flemingsberg

	DGT, Men	DGT, Women	Metabolic syndrome men	Metabolic syndrome women
	OR (CI)	OR (CI)	OR (CI)	OR (CI)
Pain	1.27 (0.48-3.38)	1.10 (0.49-2.49)	1.72 (0.66-4.52)	0.48 (0.20-1.14)
Depression	0.55 (0.15-2.03)	0.50 (0.20-1.22)	1.88 (0.61-5.79)	0.30 (0.12-0.77)
Anxiety	1.01 (0.32-3.19)	0.55 (0.24-1.25)	0.83 (0.27-2.58)	0.51 (0.22-1.19)
Sleeping-problems	0.67 (0.21-2.20)	0.80 (0.35-1.79)	1.10 (0.37-3.27)	0.64 (0.28-1.47)
Fatigue	1.60 (0.60-4.31)	0.80 (0.36-1.81)	1.92 (0.72-5.11)	0.54 (0.23-1.25)
Alcohol	2.60 (0.95-7.15)	2.27 (0.57-9.13)	0.68 (0.26-1.79)	1.32 (0.22-7.96)
Smoking	2.82 (0.90-8.86)	1.03 (0.48-2.23)	0.92 (0.32-2.69)	1.76 (0.78-3.97)
Alcohol and smoking	3.58 (1.29-9.96)	6.45 (1.06-39.32)	0.45 (0.15-1.31)	2.17 (0.29-16.04)
Education				
Low	0.18 (0.02-1.60)	1.10 (0.43-2.81)	1.34 (0.31-5.80)	1.57 (0.64-3.82)
Middle	3.61 (1.15-11.37)	0.90 (0.42-1.95)	0.69 (0.31-1.54)	0.95 (0.35-2.54)
High	0.44 (0.13-1.51)	1.08 (0.35-3.35)	0.90 (0.29-2.77)	1.02 (0.23-4.59)
Non-employed/long-term sick-leave*	0.40 (0.09-1.72)	0.40 (0.16-1.03)	1.60 (0.46-5.63)	1.00 (0.41-2.41)
Employed*	2.53 (0.58-10.99)	2.73 (1.05-7.05)	0.62 (0.18-2.19)	1.10 (0.45-2.67)
Poor selfreported Health	1.62 (0.60-4.39)	1.09 (0.46-2.61)	0.79 (0.31-2.02)	0.71 (0.24-2.06)

New DGT; Newly detected Disturbed Glucose Tolerance (new DM, IGT and IFG together)

*N = 222, age ≥65 years are not included.

5 DISCUSSION

5.1 MAIN FINDINGS

The prevalence of self-reported diabetes was higher among Turkish women living in Sweden (but not among men), compared to Swedish controls. This higher prevalence was associated with a low level of education, low rate of employment and high BMI. Also, the prevalence of stress symptoms, such as anxiety, sleeping problems, and severe pain, was higher among the Turkish men and women in Sweden compared to Swedish controls.

The Turkish immigrants in Flemingsberg exhibited twice the prevalence of diabetes and IGT compared to Turkish controls in Konya. We also found gender differences in predominant risk factors for DGT. Hypertension, alcohol consumption and smoking were the predominant risk factors among men, while high fasting TG and central obesity were the predominant risk factors among women. Stress symptoms were not associated with DGT or the metabolic syndrome, while employment was associated with DGT among Turkish women in Flemingsberg.

5.2 STRENGTHS AND LIMITATIONS

There are several strengths in this thesis. Study I and II were based on self-reported data from unique face-to-face interviews in one of the largest and most comprehensive surveys outside the USA. Official Statistics of Sweden has carried out several validation studies showing a high validity in their surveys. The consistency, comprehensiveness and high validity in the combined survey used in Study I and II is therefore a major strength in this thesis.

Study III, IV and V were based on laboratory verified data, which have a higher validity than self-reported data. All anthropometric and blood-pressure measurements for study III, IV and V, were performed by the same person.

Study I and II were the first studies to show higher odds of self-reported diabetes among Turkish-born immigrant women in Sweden and higher self-reported odds of anxiety, sleeping problems and severe pain among Turkish-born men and women in Sweden compared to Swedish controls. Further support for the relevance of increased self-reported anxiety, sleeping problems and severe pain was the proportional increase in the use of psychoactive and analgesic drugs.

Study III was the first study of laboratory verified diabetes and IGT in Turkish immigrants, with consistent methods, comparing prevalence in country of origin with country of immigration to, indicating an effect of migration. This finding has later been confirmed by similar studies in other countries.

The major limitations of this thesis are the risk of selection-bias because of the large non-response-rate, a possibility of bias from self-reported data and the limited sample size of the studied Turkish population in Flemingsberg. The cross-sectional design makes it difficult to draw inferences about causal directions between predictors and outcomes.

Size of study group. A larger study group might have been desirable in studies III, IV and V. However, the studied group comprised the total population of Turkish

immigrants in Flemingsberg. In spite of the limited sample size, the studies provided clinically relevant information about risk factors contributing to the development of diabetes as well as about gender differences.

Participation rates are known to be low among Turkish immigrants, underscoring the importance of analysing non-respondents. In Study III, IV and V the response rate was 55% of the total study population. In Study I and II, 66% among the Turkish-born immigrants in Sweden responded. In Study I and II, the age distribution among non-respondents and respondents were the same, while in Study III, IV and V, non-respondents were younger and reported a lower rate of diabetes. After adjustment for age between non-responders and responders, there was no difference in self-reported diabetes (OR 1.19, $p = 0.69$). Poor health is more common in non-respondents as shown in a large study, where the non-respondents were more often male, aged under 40 years, living alone, less educated, of poorer health, reported an unhealthy lifestyle and had either a low or a high BMI [119].

This is supported by analysis of non-respondents in Study I and II, showing lower income among non-respondents than the respondents. It can therefore be assumed that the prevalence of poor health was underestimated among Turkish-born immigrants in Sweden, especially men.

Selection bias. Low participation rate can also result in selection bias. Although non-respondents have been shown to exhibit poorer health, it is possible that respondents had a stronger incentive to participate in the study if they had a family history of diabetes. However, we found no significant differences when comparing self-reported diabetes and history of heredity of respondents with non-respondents and there was no significant difference in history of heredity when comparing those with IGT to those without IGT ($p = 0.65$).

In study III, the findings were an almost doubled increase in the prevalence of diabetes in the Turkish immigrant women (12.8% vs. 7.6%) and more than tripled prevalence of IGT in Turkish immigrant men in the Turkish immigrant group in Sweden (17.8% vs. 4.9%) compared to Turkish controls in Turkey. This raises the question whether there could have been a selection bias due to selective migration.

The reason for choosing the Konya-area for comparison was that approximately 90% of the respondents in the Turkish immigrant group in Flemingsberg originate from there and prevalence varies between different regions in Turkey [114]. It was very difficult to attain information about Kurdish descent in this area from Turkish authorities and when asking the participants in the Swedish group for their reason for migration the answers were that they came mainly as spouses and labour immigrants rather than refugees, indicating that migration was voluntary and not forced. Many spoke both Kurmanji (a Kurdish dialect) and Turkish and intermarriages were not uncommon, although many upheld the tradition to find spouses within the wider family (which in its turn could add to a genetic vulnerability). The self-reported heredity of diabetes was higher in the Turkish immigrant group in Sweden compared to Turkey. This might be explained by the awareness of type 2 diabetes in Flemingsberg, due to information campaigns, leading to an interest to ask relatives.

Had there been a selection bias in Study III, it can be assumed that the risk factors for diabetes, such as obesity and central obesity, would not be as comparable among the Turkish immigrant group in Sweden and the controls in Turkey.

Since hypertension is an important risk factor for diabetes, it is surprising that women in Turkey had a higher rate of hypertension, while diabetes was more prevalent among the Turkish women in Sweden. It is notable, however, that the mean systolic blood pressure was higher in the Swedish group, indicating the possibility of stress. Most of the tallest immigrants were born in Sweden or moved to Sweden before adolescence with a possible effect on height by regular maternity-controls and a healthier nutrition-status in Sweden. After adjustment for age at immigration, there was no significant difference in height between the population in Konya and the study population in Flemingsberg, ruling out selection bias in this aspect.

Low educational level is usually associated with higher prevalence of diabetes, however the educational level was higher among the Turkish population in Flemingsberg, than among the Turkish controls, with a lower proportion illiterate and higher proportion high school graduates in Sweden. The reason for this could be the Swedish language program for immigrants and the high proportion of high school graduates among the young Turkish second-generation immigrants or the migration of skilled Turkish workers to Sweden (according to Akgündüz). The higher prevalence of diabetes and IGT in Sweden could therefore not be explained by low educational level.

Conceptual and contextual equivalence. In intercultural studies, it is important to avoid bias due to conceptual and contextual differences. The instrument measuring the same theoretical construct in the different cultures has to be validated. Translations must be in lay terminology [120] and unfortunately, there was no description of how issues of conceptual equivalence were handled in Study I and II, only that questionnaires were translated by professional translators. Considering that almost 80% of the interviews were performed in Swedish, the question also is how the Turkish-born immigrants comprehended the Swedish words used in the questionnaire.

It is important not only when comparing self-reported data but also when designing studies in Sweden for the Turkish immigrant group, to have knowledge of possible contextual differences between the Turkish and Swedish culture. This is very well described in Lisbeth Sachs book based on her thesis “Evil Eye or Bacteria: Turkish migrant women and Swedish health care”, where the adaptation process that women and their children from Central Anatolia undergo after moving to Sweden is studied. This process is not always what we expect and can complicate the meeting with health care services when illness is the dominating cause of consultation and the patient expects a treatment intended for a disease. If the Turkish women felt misunderstood, they felt ignored and could exaggerate symptoms. They often experienced their health worse in Sweden compared to when they lived in Kulu, a town in the district Konya in Turkey. In Kulu, women presented their illness influenced by socio-cultural specific symptoms and had therefore not disease in their ideas. Practitioners of traditional medicine in their health care system did likewise, and the Turkish doctors often based their treatments on illness, rather than on disease. After migration to Sweden, their role repertoire changed and this often led to physical symptoms [121]. In Study V, the finding of a higher prevalence of DGT in working Turkish women in Flemingsberg, could be associated with this change of role repertoire involved in the acculturation process adding to accultural stress and allostatic load. The tendency to express psychological illness with physical symptoms was also shown in a study on Turkish women in Sweden where pain was the prominent symptom, often lateralised to one side of the body, with spreading (which was regarded as a bad sign). To seek psychiatric

consultation was regarded as shameful and rarely accepted or valued as tool for recovery [122]. In a study in Britain, comparing depressive symptoms, the frequency and severity of individual symptoms showed higher mean ratings in the British sample for core depressive symptoms and higher ratings in the Turkish sample for symptoms reflecting somatization and a tendency to emphasize symptoms. Another study showed that immigrant patients live under more strained psychosocial conditions and experience a deeper impact of pain than Swedish-born patients [90]. These findings indicate that there are some similarities in the symptoms of depression in the two cultures, but also differences in their predominant mode of expression [123]. In another study, the non-acculturated Turkish group showed more psychic symptoms (depression, loss of interest, hypersensitivity) than the acculturated group [124]. Although there might be a cultural way to express physical and mental symptoms, there are plenty of studies comparing Turkish immigrants to the indigenous population addressing the Turkish immigrant morbidity regarding diabetes [103, 108, 125, 126].

Bias in self-reported data. Self-reported diabetes has been found to show higher sensitivity (67%) and specificity (95%) than self-reported heart disease or hypertension [127] [128]. The correlations between self-reported and measured BMI has been found to be high, even if there is a tendency for erroneous self-reporting of a “slim-body shape” [129, 130], however this can be adjusted for [129]. We did not assume any discrepancies between self-reported and measured levels of BMI and obesity between Turkish-born and the Swedish controls in Study I, however a recent study, comparing Turkish and Moroccan women with Dutch controls, showed differences in the discrepancies between self-reported and measured levels of BMI and obesity [131]. If there would be similar discrepancies in study I, and adjustment would be performed, BMI would be even higher in the Turkish group.

The Turkish immigrants in Study I reported a lower rate of hypertension than the Swedish controls. This was consistent with results from a study of cardiovascular risk factors among immigrants in Sweden [132].

5.3 PREVALENCE (STUDIES I, II AND III)

It is reasonable to assume that the risk of bias in Study I and II is low and that the well validated survey widely used internationally and constructed to give an objective response, are comparable between the studied groups. Therefore, the validity of self-reported diabetes, anxiety, sleeping-problems and severe pain is high. The findings regarding anxiety, sleeping problems and pain, as well as the gender differences in prevalence of diabetes, are in agreement with studies from other countries [114, 133]. Also in line with our results, are the findings in a study, based on the same data set as studies I and II, which found that Turkish immigrants had a higher risk of reporting poor self-rated-health compared to Swedish controls [85] which also is in line with our findings.

Self-reported diabetes prevalence in Study I compared to prevalence in Study III
The relative low rate of self-reported diabetes in study I compared to self-reported diabetes study III (study I: men 2.1%, women 3.3% vs. study III: men 6.7%, women 10.8%) is mainly explained by the age difference with a younger population in study I. Furthermore the immigrants who had stayed in Sweden more than 15 years were excluded in study I. It is possible that the acculturation process during the longer

residence in Sweden (study III mean: 23 years) led to changes in lifestyle, which may have caused higher prevalence of diabetes. Increased knowledge among health-care professionals about earlier onset and higher prevalence of diabetes in the Turkish immigrant group could also lead to earlier detection due to more frequent testing (participants in study III).

While selection-bias in immigration to Sweden and self-selection among those participating in the study remains a possible confounding factor, the Turkish immigrants in Flemingsberg, to the best of our ability to determine, correspond well to the Konya population as well as to the overall Turkish immigrant population in Sweden as far as reasons for migration and ethnic background.

The findings of a higher prevalence of diabetes among the women compared to men in the Swedish immigrant group in study III, is in line with other studies, which have shown high prevalence of diabetes among immigrants from the Middle East, including from Turkey [104, 105, 134]. For example, in a study performed in Norway, a country similar to Sweden, a diabetes prevalence of 11.9% was found in Turkish women and 12% in Turkish men [135] (similar prevalence, although not higher among women).

5.4 PREDOMINANT RISK FACTORS AND GENDER DIFFERENCES (STUDIES IV AND V)

There were significant gender differences in the prevalence of risk factors in the Turkish immigrant group in Flemingsberg. Hypertension and smoking were the most prominent risk factors among men, while central obesity and high fasting TG were more prominent among women.

Smoking/former smoking was associated with increased OR for DGT among the men in our study group. The opposite finding has been for smokers only in a study in Turkey [114]. A reason for the higher odds for the former smoking group could be weight gain after smoking cessation.

It has been argued that central obesity with a waist girth of 83 cm or greater is one of the most important risk factors for diabetes among Turkish women [136]. The prevalence of central obesity with waist-measure of ≥ 88 cm was similar for Turkish women in Sweden (41.9%) as in a study on Turkish women in Turkey (38.9%) [137], yet the prevalence of diabetes among Turkish women in Sweden was significantly higher than among women in Turkey. Central obesity among the women can therefore only partly explain the high prevalence of diabetes and IGT. The prevalence of diabetes and IGT is proportionally much higher than the prevalence of central obesity [114, 138, 139] and the metabolic syndrome [140-142] in Turkish women in Flemingsberg, when compared with other studies.

Our findings regarding gender differences in prevalence of the metabolic syndrome also seems to be corroborated in the literature, depending on which tool is used. With the ATPIII definition, women seemed to have higher prevalence of the metabolic syndrome than men, while, with WHO criteria, the prevalence was higher in men [40].

The finding of high occurrence of elevated TG and low HDL was also mirrored in the results of a Norwegian study on immigrants including Turkish immigrants [143]. In our study this “diabetic dyslipidaemia” was prevalent among those with diabetes (unpublished data).

5.5 STRESS

One of the aims in this thesis was to study whether there were any associations between stress symptoms, expressed as depression, anxiety, sleeping problems, fatigue and pain with disturbed glucose tolerance and the metabolic syndrome. No significant association was found. An expected finding was that alcohol consumption together with smoking was significantly associated with newly diagnosed DGT. Surprisingly, and contrary to many studies, we found a negative association between depression and the metabolic syndrome among the women. The higher OR for the association between being employed and new DGT among women was also surprising. In the Norwegian HUNT study, similarly to our results, no association was found between depression or anxiety and the metabolic syndrome [144]. Also in a study in the Netherlands, no association was found between anxiety and glucose metabolism. Depressive symptoms were mainly manifested in participants with type 2 diabetes in another study, not with participants with impaired glucose metabolism [145].

Contrary to our findings, higher rates of obesity and glucose intolerance among women in Turkey in the TURDEP-study, were suggested to be caused by lack of employment [114]. One explanation why new DGT in our material was associated with employment, could be the change of role repertoire (according to Sachs), stressful or poor working-conditions and that the Turkish women are traditionally taking more responsibility for the household and could experience stress/acculturative stress related to this double work [146]. Poor working conditions such as low decision latitude was associated with type 2 diabetes in one study on Swedish middle-aged women[147].

In this study, even when adding the stressors together (Brant test of Parallel Regression Assumption), there was no significant trend for new DGT or the metabolic syndrome. This could be due to the fact that the study group was small, however other findings were significant. We excluded those with known diabetes since they often have intervention and having the disease could also cause concerns and worries. By analysing a combined group with IGT and IFG together with newly diagnosed diabetes, the study-group became larger which could dilute the results, however concerning intervention it is also important to address those in risk of developing diabetes. Smoking and using alcohol could be associated with stress and are well known risk factors for diabetes.

Numerous studies have shown associations between waist circumference, cardiovascular risk factors, diabetes and psychological distress/depression, however some studies have revealed genetic/ethnic differences in those associations. For example one study showed a stronger association between obesity and depression among Caucasians than among African Americans or Hispanics in the US population [148, 149]. Furthermore in a study from The Netherlands on Turkish immigrants, there was a higher rate of psychological distress and diabetes compared to the Dutch group, but no association between depression and cardiovascular risk factors [150]. Our findings are similar.

The mean onset of diabetes in study IV was at 46 years among women and 47 years among men. A Dutch study showed that the Turkish immigrants had an onset of diabetes 10 years earlier than the indigenous population [108]. In a study on diabetes onset in Middle East immigrants compared to Swedish-born patients onset was 12 years earlier in the immigrants (43 vs 55 years) and that early onset of diabetes was

associated with a more severe reduction in pancreatic B-cell function [109]. This underlines the importance of finding these patients timely.

5.6 CONCLUSIONS, IMPLICATIONS

From the main findings in this thesis, it can be concluded that there is more DGT among Turkish immigrants in Sweden than both among Swedish controls (the women) as well as among Turkish controls in Turkey. This appears to be a negative effect of migration to Sweden, not related to commonly implicated stress factors.

The findings in this thesis with a high prevalence of DGT among the Turkish immigrants in Sweden, although similar rate of BMI, obesity and the metabolic syndrome when compared to Turkey, raised the question whether migration and stress could contribute to the high prevalence of diabetes in the Turkish immigrant group in Sweden. Since neither DGT nor the metabolic syndrome was associated with stress symptoms in the Turkish group in Sweden, it remains to study other risk factors. In a study in type 2 diabetes patients from the Middle-East (including Turkey), clinical characteristics were compared with Swedish controls and showed earlier onset, stronger family history and more rapid decline of pancreatic B-cell function in the Turkish patients, suggesting a different form of type 2 diabetes compared with Swedish patients [109]. Earlier onset and a strong family history could be caused by genetic diabetes susceptibility, perhaps another type of diabetes than in the Swedish population. The migration to Sweden with rapid lifestyle change and living in deprived Swedish neighborhood could hasten the development of diabetes.

While the studied life-style factors can only partially explain our findings, this thesis demonstrates important implications for the clinical management as well as for intervention programs.

Further studies of other possible contributing factors will add clarity to the direction of interventions in this immigrant subpopulation.

These findings, regardless of cause, have important implications for public health planning in Sweden. Physical activity is low especially among the women. Although not finding any significant odds for diabetes IGT or IGF in those who were physically inactive, the whole group in Flemingsberg should be regarded as a risk group, especially the women, since evidence regarding physical inactivity and diabetes are substantial. High blood pressure, tobacco use, high blood glucose, physical inactivity, overweight and obesity, are responsible for the increasing risks of chronic non-communicable diseases such as heart disease, diabetes and cancers and are the leading global risk factors for mortality in all income groups worldwide [13]. Concerning risk factors and the previously described causal chain, to modify several background causes will likely have amplifying effects and result in sustained improvements to health. In the Health Care Centre in Flemingsberg where the survey was performed, all participants with DGT received written information about life style changes. Smoke cessation and weight reducing programmes were offered, especially designed for the Turkish group with Turkish interpreters when needed. Nordic Walking groups were especially popular among the women.

Our findings illustrate the need for an integrated approach, not only from the health care providers, as the analyses suggest that a reason for the high prevalence of both diabetes and its risk factors is partly a lack of acculturation. Barriers to this are

language problems, and low educational level among Turkish immigrant women. Special efforts must be made on different levels when developing intervention programmes in order to reduce inequalities in health between native-born Swedes and Turkish-born immigrants. Turkish immigrants in Sweden should be considered a risk group, and early detection is of utmost importance to prevent long-term complications. Overweight with central obesity, hypertension, alcohol, smoking and physical inactivity, especially among the women, should also be targeted. Finally, culturally adjusted and gender specific information on prevention should be developed and distributed to this target group.

5.7 FUTURE METHODS AND STUDIES

Future follow-up studies on the cohort of Turkish immigrant in Flemingsberg are planned. Subjects with IGT and diabetes were included in intervention programs.

5.7.1 Screening with HbA1c

OGTT is costly and troublesome for the participant. A test with HbA1c is easier and less expensive than OGTT and has recently been added as a tool of diagnostics (not in children or in cases of suspected type 1 diabetes), (Table 8). A review of several studies have shown a 5-year incidence of diabetes ranging from 9-25% for an HbA1c range of 5.5–6.0% DCCT (37-42 mmol/mol IFCC) compared with 25-50% for an HbA1c of 6.0–6.5% DCCT (42-48 mmol/mol IFCC) [33]. In studies on populations from China, Japan, Korea, Middle East, US and Australia it has been shown that HbA1c is less sensitive but more specific when compared to FPG or OGTT as diagnostic tools [151-157]. In summary, interventions should be most intensive in the category with an HbA1c > 6.0, however the most appropriate specific cut-point for defining IFG with FBG is still being debated [158].

OGTT was used in the first TURDEP-study and our study III was designed for a comparison with TURDEP-data from Konya. In the second TURDEP-study (TURDEP-II) OGTT, FPG or HbA1c test alone could only detect 65, 56 and 40% of new diabetes. New diabetes detected by FPG had a mean HbA1c level of 6.6% (49 mmol/mol). Corresponding value for new diabetes diagnosed by OGTT was 5.9% (41 mmol/mol), however new diabetes detected only by HbA1c screening had a mean HbA1c level of 7.6% (60 mmol/mol) [133]. In our material we found similar mean levels for HbA1c. Therefore screening with HbA1c is not optimal for finding IGT or IGF in Turkish subjects. This has been confirmed in a study on patients with Arabic descent, where the use of HbA1c showed a high number of false negative tests suggesting ethnic/genetic differences using A1C-based criteria for diagnosis and prediction of diabetes [154]. This has to be considered in future studies of the Turkish immigrant group in Sweden.

Table 8 – Criteria for diabetes, pre-diabetes, impaired fasting glucose (IFG), impaired glucose tolerance (IGT) and gestational diabetes mellitus (GDM) according to the American Diabetes Association (ADA), International Diabetes Federation (IDF), the World Health Organization (WHO) and The International Association of Diabetes and Pregnancy Study Groups (IADPS) (criteria not used in Sweden at the moment).

	FPG	2-hr PG	HbA1c
Diabetes Mellitus (ADA, IDF, WHO)	≥ 7.0 mmol/l	or ≥ 11.1 mmol/l	or ≥ 6.5% DCCT (≥48 mmol/mol). IFCC
Prediabetes (ADA)	5.6 -6.9 mmol/l (IFG)	or 7.8 -11.0 mmol/l (IGT)	or 5.7–6.4% DCCT (39–46 mmol/mol) IFCC
IFG (isolated) (WHO)	6.1-6.9mmol/l	and <7.8mmol/l	
IGT (WHO)	<7.0mmol/l	and ≥7.8 and <11.1mmol/l.	
GDM screening at 24-28 weeks (IADPSG)	≥ 5.1 mmol/l	or 1 hr: ≥10.0 mmol/l or 2 hr: ≥ 8.5 mmol/l).	

5.7.2 Physical activity

Study I showed that low levels of physical activity was more common in Turkish immigrant women than in Swedish women and study IV showed a high level of self-reported physical inactivity, especially in the Turkish women in Flemingsberg. Other methods with higher accuracy than self-reported data suitable for large-scale population studies should be considered. Body motion sensing by accelerometry, heart rate monitoring, pedometry and room calorimetry (a highly accurate method but expensive), are methods that could be considered in the future [23].

5.7.3 Dietary factors

Results from our data (unpublished) showed that a majority of the Turkish immigrants in Flemingsberg reported that they mainly maintained traditional Turkish dietary habits, which agrees with previous studies that have shown that younger members of Turkish origin continue to value their traditional food cultures. When using 24 h dietary recalls one has to be aware of cultural differences in self-reporting. One study noticed a significant underreporting in Turkish immigrants compared to Swedish controls [159, 160]. Signs of oxidative stress have been shown in Turkish immigrant women in Sweden, levels of F2-isoprostane (marker for oxidative stress) were higher in The Turkish women than in Iranian and Swedish women [161]. Future studies should include qualitative focus group discussions and/or well validated and culturally adjusted surveys including antioxidant intake, vitamin D intake and dietary glycemic load.

5.7.4 Vitamin-D-deficiency

Future studies should include vitamin-D-measurements. The association between vitamin D-deficiency and diabetes is well known and there are several studies assessing

vitamin D deficiency among Turkish immigrant groups who have moved to more northern latitudes. In a study from Norway (60 degrees latitude), there were significantly lower levels of vitamin D (, 25-hydroxycholecalciferol, 25(OH) D) among Turkish immigrants compared to Norwegians. In Germany (50 degrees latitude), a strong correlation between low 25(OH) D levels and higher rates of generalized bone and/or muscle aches and pains was found. Turkish immigrants had significant lower 25(OH) D levels compared to Turkish national residents in Turkey [162, 163]. Regarding the findings in study II, with higher odds for self-reported anxiety, sleeping problems and severe pain compared to Swedes and the findings in study III, with higher odds of diabetes and IGT in Turkish immigrants in Sweden compared to Turkish national residents, analysis of 25(OH) D might have added further information.

5.7.5 Studies on additional metabolic criteria

There seems to be a link between the metabolic and the immune systems [50], and a metabolic imbalance leads to immune imbalance, with starvation and immunosuppression in one end and obesity and inflammatory diseases in the other end. The first molecular inflammatory link found was TNF- α from adipose tissue. An overproduction of TNF- α and other inflammatory components like IL-1 and MCP-1 contributes significantly to insulin resistance. Molecules typical of adipocytes like leptin, adiponectin, resistin, and visfatin can also regulate the immune response. Lipids themselves also participate in the coordinate regulation of inflammation and metabolism. Elevated plasma lipid levels are characteristic of obesity, infection, and other inflammatory states. The C-reactive-protein is higher in people with obesity and is a risk marker for diabetes [50]. Future studies might include adipose tissue biomarkers (leptin, adiponectin), apolipoproteins, homeostasis model assessment (HOMA-IR), proinflammatory state (CRP, TNF- α , IL-6), fibrinolytic/clotting factors and hormonal factors (HPA-axis).

5.7.6 Microbiota

Altered gut microbiota has been linked to metabolic diseases [164]. Future studies of possible changes in microbiota by migration and/or by lifestyle-changes may give important new insights into the interaction between the human body and its colonizing microbiome.

5.7.7 Acculturation

Questions on acculturation such as knowledge of Swedish were asked in Study II, however not in Study III, IV and V and could have been added for a better connection with study II.

Poor knowledge of Swedish and high experience of discrimination could add to psychological distress factors. One possible explanation for the higher risks of anxiety, sleeping problems and pain among Turkish-born immigrants in Sweden could be stressful acculturation with a high allostatic load. Bhugra argues in the review article Migration and mental health, that migration can be very stress inducing with individual coping strategies for a number of stressors, which together with resilience and the fact whether migration is forced or voluntary, will influence the outcome. In Study III, IV

and V migration was voluntary, however the reason for migration in Study I and II is unknown. Lack of acculturation has also been shown to be a risk factor for diabetes [165].

In a study of Turkish immigrants in Sweden the conclusion was that they were not well integrated, that the Turkish immigrant group preferred to live within the boundaries of their segregated, closed, communities, in spite of Swedish integration policies. However, Turkish immigrants' quality of life perceptions were better than those of the Turkish controls in Turkey. The third generation in Sweden received the highest scores [166].

In a large survey performed by National Board of Health and Welfare on four immigrant groups, there was an association between acculturation status (knowledge of Swedish) and health [111]. Further studies on the acculturation process in different immigrant groups are of importance for a deeper knowledge of the impact of migration and acculturation on health. It is also important to identify the stage of migration since different stages have different effect on health. A review on common mental health problems in immigrants showed that their prevalence was lower in immigrants but increased over time to become similar to the general population [167] underlining the effect of acculturation.

6 SUMMARY IN SWEDISH

6.1 BAKGRUND

Förekomsten av diabetes liksom migration ökar världen över. Olika etniska grupper har olika förekomst av diabetes och det är oklart vilka riskfaktorer som är förknippade med denna skillnad.

6.2 SYFTE

Syftet med denna avhandling är att, i den turkiska invandrargruppen i Sverige, undersöka förekomsten av och riskfaktorer för diabetes, nedsatt glukostolerans och nedsatt faste blodglukos (störd glukostolerans) samt att undersöka om migration och stress (ångest, depression, sömnproblem, smärta) kan vara riskfaktorer.

6.3 METOD

De två första studierna bygger på två stora väl validerade nationella tvärsnittsstudier; Levnadsförhållanden hos Svenskar (ULF, Statistiska Centralbyrån) och Invandrarundersökningen (Invandrar-ULF), ett samarbetsprojekt mellan Socialstyrelsen, Invandrarverket, Folkhälsoinstitutet och Inrikesdepartementet. I vår undersökning analyserades de turkiska invandrarna i Sverige ($n = 526$) och jämfördes med svenska kontroller ($n = 2854$), alla i åldrarna 27-60 år.

Åldersjusterade, könsspecifika logistiska regressionsmodeller användes för att jämföra självrapporterad diabetes och stress-symtom (oro-ångest, sömnproblem och svår smärta) mellan den turkiska och den svenska gruppen. I de fullständiga modellerna ingick även utbildning, sysselsättning och BMI (jämförelse av diabetesförekomst), liksom utbildning, civilstånd och sysselsättning (jämförelse av stress-symtom).

I en tvärsnittsstudie av hela den Turkiska populationen i Flemingsberg i åldrarna ≥ 20 år intervjuades 238 Turkiska invandrare och data om sjukhistoria, fysisk inaktivitet, stress, rökning och dryckesvanor insamlades. Antropometriska mått (vikt, längd, BMI, bukomfång) och blodprover togs, blodtryck mättes och en oral glukosbelastning (OGTT) genomfördes. Data jämfördes med 1549 deltagare från Konya området i Turkiet i åldrarna ≥ 20 år.

Data från den turkiska invandrargruppen i Flemingsberg analyserades även med avseende på diabetes, nedsatt glukostolerans (IGT) och nedsatt fasteglukos (IFG), gemensamt benämnda störd glukostolerans (DGT). De riskfaktorer som studerades var högt blodtryck, övervikt, fetma, bukfetma, höga fastetriglycerid nivåer, lågt HDL-kolesterol, det metabola syndromet, rökning och alkohol konsumtion, fysisk inaktivitet, stress, försämrad självskattad hälsa, låg sysselsättningsgrad och låg utbildning.

Data analyserades genom att använda Chi-square test, t-test och könsspecifik, ålderjusterad, multivariat logistisk regression.

6.4 RESULTAT

Hos turkiska män i Sverige var den åldersjusterade diabetes prevalensen inte högre än hos svenska män, odds ratio (OR) 1,04 (95 % konfidensintervall (CI) 0,35-3,11) men hos kvinnorna var diabetes prevalensen högre hos de turkiska kvinnorna jämfört med

de svenska OR 3,22 (CI 1,36 - 7,64). Den högre förekomsten var associerad med låg utbildning, låg sysselsättning och högt BMI.

I en fullständig modell, var OR 2,12 (CI 1,43 - 3,15) för ångest, 2,60 (1,82 - 3,72) för sömnproblem och 2,14 (1,50 - 3,05) för svår smärta bland turkiska män och 2,44 (1,69 - 3,53) för ångest, 3,01 (2,09-4,33) för sömnproblem, och 2,59 (1,80-3,71) för svår smärta bland turkiska kvinnor, jämfört med de svenska kontrollerna.

Förekomsten av diabetes och IGT var signifikant högre bland turkiska invandrare i Flemingsberg (11,8% resp. 15,6%) jämfört med en kontrollgrupp i Konya i Turkiet (7,1% resp. 7,6%). Turkiska kvinnor i Flemingsberg hade högre förekomst av diabetes än turkiska kvinnor i Konya (12,8% mot 7,6%). Likaså var IGT högre bland turkiska män i Flemingsberg jämfört med män i Konya (17,8% mot 4,9%).

Diabetes debuterade relativt tidigt inom den turkiska invandrargruppen i Flemingsberg, i genomsnitt vid ca 47 års ålder. I samma grupp, efter åldersjustering i en fullständig modell, var oddsen för män 4-5 gånger högre för DGT (diabetes och IGT) om de hade högt blodtryck eller var rökare/före detta rökare. Central fetma och höga faste-triglycerider, gav oberoende av varandra, 4,5 gånger högre odds för DGT bland kvinnorna.

Vi fann inget samband mellan nyupptäckt DGT (nydiagnostiserad diabetes, IGT och IFG) eller det metabola syndromet, och stressfaktorer som smärta, depression, ångest, sömnproblem, trötthet eller självrapporterad dålig hälsa. Alkoholkonsumtion i kombination med rökning däremot visade tre gånger högre odds för nyupptäckt DGT jämfört med de som ej rökte eller drack alkohol (OR 3,58 CI 1,29-9,96), bland de turkiska männen i Flemingsberg. Vi fann även tre gånger högre odds för nyupptäckt DGT bland de turkiska kvinnor i Flemingsberg som var i arbete jämfört med de som ej arbetade (OR 2,73 CI 1,05-7,05)

6.5 SLUTSATSER

Förekomsten av självrapporterad diabetes var högre bland turkiska kvinnor i Sverige jämfört med svenska kvinnor, vilket var associerat med lägre sysselsättningsgrad, lägre utbildningsnivå och en högre grad av övervikt och fetma. De turkiska invandrarna i Sverige hade signifikant ökad självrapporterad ångest, sömnproblem och svår smärta jämfört med svenska kontroller, även efter justering för ålder och socioekonomisk faktorer. Den nästan dubblade förekomsten av diabetes och IGT bland turkiska invandrare i Flemingsberg, jämfört med kontroller i Konya, tyder på att migrationen är associerad med diabetes och de turkiska invandrarna utgör en särskild riskgrupp. Den relativt tidiga diabetesdebuten är en riskfaktor och de dominerande riskfaktorerna varierar beroende på kön. Stress verkar inte vara associerat med den höga förekomsten av DGT i den turkiska invandrargruppen i Flemingsberg. Att vara en turkisk invandrare i Sverige är en riskfaktor i sig för DGT. De funna riskfaktorerna kan inte förklara den höga förekomsten av DGT varför det finns behov av ytterligare studier med focus på migration och ackulturations potentiella riskfaktorer (livsstilsförändringar, D-vitamin-brist, förändrad tarmflora). I nuläget bör man inrikta sig på övervikt, högt blodtryck, alkohol och rökning som riskfaktorer vid utformandet av kulturellt och genusanpassade interventionsprogram för de turkiska invandrarna i Sverige.

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